(19) World Intellectual Property Organization

International Bureau



(43) International Publication Date 9 September 2005 (09.09.2005)

PCT

(10) International Publication Number WO 2005/082398 A2

(51) International Patent Classification7:

A61K 38/00

(21) International Application Number:

PCT/US2005/005596

(22) International Filing Date: 24 February 2005 (24.02.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/547,512 26 February 2004 (26.02.2004) US 60/579,342 15 June 2004 (15.06.2004)

(71) Applicants (for all designated States except US): OHIO UNIVERSITY [US/US]; Technology Transfer Office, 20 East Circle Drive, Athens, GA 45701 (US). ICORIA, INC. [US/US]; 108 T.W. Alexander Drive, P.O. Box 14528, Research Triangle Park, NC 27709 (US).

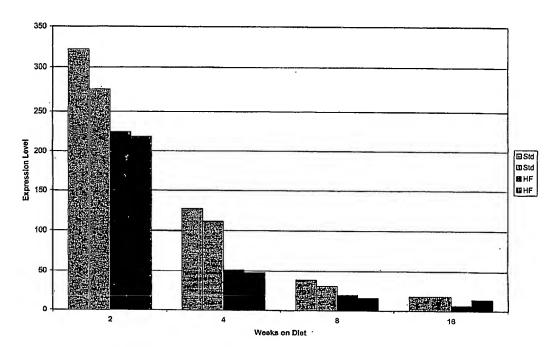
(72) Inventors; and

(75) Inventors/Applicants (for US only): KOPCHICK, John, J. [US/US]; 4 Orchard Lane, Athens, OH 45701 (US). COSCHIGANO, Karen, T. [US/US]; 11703 Channingway Blvd., The Plains, OH 45780 (US). BOYCE, Keith, S. [US/US]; 2589 Cole Road, Wexford, PA 15090 (US). KRIETE, Andres [US/US]; 1222 Driftwood Drive, Pittsburgh, PA 15243 (US).

- (74) Agents: BROWDY, Roger, L. et al.; Browdy and Neimark, P.L.L.C., Suite 300, 624 Ninth Street N.W., Washington, DC 20001-5303 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

[Continued on next page]

(54) Title: DIAGNOSIS OF HYPERINSULINEMIA AND TYPE II DIABETES AND PROTECTION AGAINST SAME BASED ON GENES DIFFERENTIALLY EXPRESSED IN MUSCLE CELLS



(57) Abstract: Mouse genes differentially expressed in comparisons of normal vs. hyperinsulinemic, hyperinsulinemic vs. type 2 diabetic, and normal vs. type 2 diabetic muscle by gene chip analysis have been identified, as have corresponding human genes and proteins. The human molecules, or antagonists thereof, may be used for protection against hyperinsulinemia or type 2 diabetes, or their sequelae.

WO 2005/082398 A2



SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Published:

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DIAGNOSIS OF HYPERINSULINEMIA AND TYPE II DIABETES AND PROTECTION AGAINST SAME BASED ON GENES DIFFERENTIALLY EXPRESSED IN MUSCLE CELLS (15.1)

Cross-Reference to Related Applications

Anti-Aging Applications. Mice with a disrupted growth hormone receptor/binding protein gene enjoy an increased lifespan. In U.S. Prov. Appl. 60/485,222, filed July 8, 2003 (Kopchick8) mouse genes differentially expressed in comparisons of gene expression in growth hormone receptor/binding protein gene-disrupted mouse livers and normal mouse livers were identified, as were corresponding human genes and proteins. It was suggested that the human molecules, or antagonists thereof, could be used for protection against faster-than-normal biological aging, or to achieve slower-than-normal biological aging. It was also taught that the human molecules may also be used as markers of biological aging.

In provisional application Ser. No. 60/474,606, filed June 2, 2003 (our docket Kopchick7-USA) , our research group used a gene chip to study the genetic changes in the liver of C57Bl/6J mice that occur at frequent intervals of the aging process. Differential hybridization techniques were used to identify mouse genes that are differentially. expressed in mice, depending upon their age. The level of gene expression of approximately 10,000 mouse genes (from the Amersham Codelink UniSet Mouse I Bioarray, product code: 300013) in the liver of mice with average ages of 35, ... 49, 56, 77, 118, 133, 207, 403, 558 and 725 days was determined. In essence, complementary RNA derived from mice of different ages was screened for hybridization with oligonucleotide probes each specific to a particular mouse gene, each gene in turn representative of a particular mouse gene cluster (Unigene). Mouse genes which were differentially expressed (younger vs. older), as measured by different levels of hybridization of the respective CRNA samples with the particular probe corresponding to that mouse gene, were identified. Related human genes and proteins were identified by sequence comparisons to the

mouse gene or protein. In the international appl.

Kopchick7A-PCT, filed June 2, 2004, we added some additional studies of CIDE-A (see below).

In a like manner, the effect of aging on the expression of genes in mouse skeletal muscle was studied, see provisional application Ser. No. 60/566,068, filed April 29, 2004 (our docket Kopchick14-USA).

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Anti-Diabetes Applications. In U.S. Provisional Appl. Ser. No. 60/458,398 (our docket Kelder1-USA), filed March 31, 2003, members of our research group describe the identification of genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse liver. Forward- and reverse-substracted cDNA libraries were prepared, clones were isolated, and differentially expressed cDNA inserts were sequenced and compared with sequences in publicly available sequence databases. The corresponding mouse and human genes and proteins were identified.

The purpose of our research group's provisional application Ser. No. 60/460,415 (our docket: Kopchick6-USA), filed April 7, 2003, was similar, but complementary RNA, derived from RNA of mouse liver, was screened against a mouse gene chip. See also 60/506,716, filed Sept. 30, 2003 (Kopchick6.1).

Gene chip analyses have also been used to identify genes differentially expressed in normal vs. hyperinsulinemic, hyperinsulinemic vs. type II diabetic, or normal vs. type II diabetic mouse pancreas, see U.S. Provisional Appl. 60/517,376, filed Nov. 6, 2003 (Kopchick12) and muscle, see U.S Provisional Appl. 60/547,512, filed Feb. 26, 2004 (Kopchick15).

Other differential hybridization applications. The use of differential hybridization to identify genes and proteins is also described in our research group's Ser. No. PCT/US00/12145 (Kopchick 3A-PCT), Ser. No. PCT/US00/12366 (Kopchick4A-PCT), and Ser. No. 60/400,052 (Kopchick5).

All of the foregoing applications are hereby incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to various nucleic acid molecules and proteins, and their use in (1) diagnosing hyperinsulinemia and type II diabetes, or conditions associated with their development, and (2) protecting mammals (including humans) against them.

Description of the Background Art

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Diabetes

A deficiency of insulin in the body results in diabetes mellitus, which affects about 18 million individuals in the United States. It is characterized by a high blood glucose (sugar) level and glucose spilling into the urine due to a deficiency of insulin. As more glucose concentrates in the urine, more water is excreted, resulting in extreme thirst, rapid weight loss, drowsiness, fatigue, and possibly dehydration. Because the cells of the diabetic cannot use glucose for fuel, the body uses stored protein and fat for energy, which leads to a buildup of acid (acidosis) in the blood. If this condition is prolonged, the person can fall into a diabetic coma, characterized by deep labored breathing and fruity-odored breath.

There are two types of diabetes mellitus, Type I and Type II. Type II diabetes is the predominant form found in the Western world; fewer than 8% of diabetic Americans have the type I disease.

Type I diabetes. In Type I diabetes, formerly called juvenile-onset or insulin-dependent diabetes mellitus, the pancreas cannot produce insulin. People with Type I diabetes must have daily insulin injections. But they need to avoid taking too much insulin because that can lead to insulin

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shock, which begins with a mild hunger. This is quickly followed by sweating, shallow breathing, dizziness, palpitations, trembling, and mental confusion. As the blood sugar falls, the body tries to compensate by breaking down fat and protein to make more sugar. Eventually, low blood sugar leads to a decrease in the sugar supply to the brain, resulting in a loss of consciousness. Eating a sugary food can prevent insulin shock until appropriate medical measures can be taken.

Type I diabetics are often characterized by their low or absent levels of circulating endogenous insulin, i.e., hypoinsulinemia (1). Islet cell antibodies causing damage to the pancreas are frequently present at diagnosis. Injection of exogenous insulin is required to prevent ketosis and sustain life.

Type II diabetes. Type II diabetes, formerly called adult-onset or non-insulin-dependent diabetes mellitus (NIDDM), can occur at any age. The pancreas can produce insulin, but the cells do not respond to it.

Type II diabetes is a metabolic disorder that affects approximately 17 million Americans. It is estimated that another 10 million individuals are "prone" to becoming diabetic. These vulnerable individuals can become resistant to insulin, a pancreatic hormone that signals glucose (blood sugar) uptake by fat and muscle. In order to maintain normal glucose levels, the islet cells of the pancreas produce more insulin, resulting in a condition called hyperinsulinemia. When the pancreas can no longer produce enough insulin to compensate for the insulin resistance, and thereby maintain normal glucose levels, hyperglycemia (elevated blood glucose) results, and type II diabetes is diagnosed.

Early Type II diabetics are often characterized by hyperinsulinemia and resistance to insulin. Late Type II diabetics may be normoinsulinemic or hypoinsulinemic. Type II diabetics are usually not insulin dependent or prone to ketosis under normal circumstances.

Little is known about the disease progression from the

normoinsulinemic state to the hyperinsulinemic state, and from the hyperinsulinemic state to the Type II diabetic state.

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As stated above, type II diabetes is a metabolic disorder that is characterized by insulin resistance and impaired glucose-stimulated insulin secretion (2,3,4). However, Type II diabetes and atherosclerotic disease are viewed as consequences of having the insulin resistance syndrome (IRS) for many years (5). The current theory of the pathogenesis of Type II diabetes is often referred to as the "insulin resistance/islet cell exhaustion" theory. According to this theory, a condition causing insulin resistance compels the pancreatic islet cells to hypersecrete insulin in order to maintain glucose homeostasis. However, after many years of hypersecretion, the islet cells eventually fail and the symptoms of clinical. diabetes are manifested. Therefore, this theory implies that, at some point, peripheral hyperinsulinemia will be an antecedent of Type II diabetes. Peripheral hyperinsulinemia can be viewed as the difference between what is produced by \ the β cell minus that which is taken up by the liver. Therefore, peripheral hyperinsulinemia can be caused by increased β cell production, decreased hepatic uptake or some combination of both. It is also important to note that it is not possible to determine the origin of insulin resistance once it is established since the onset of peripheral hyperinsulinemia leads to a condition of global insulin resistance.

Multiple environmental and genetic factors are involved in the development of insulin resistance, hyperinsulinemia and type II diabetes. An important risk factor for the development of insulin resistance, hyperinsulinemia and type II diabetes is obesity, particularly visceral obesity (6,7,8). Type II diabetes exists world-wide, but in developed societies, the prevalence has risen as the average age of the population increases and the average individual becomes more obese.

problem in the United States. Obesity-related health risks include high blood pressure, hardening of the arteries, cardiovascular disease, and Type II diabetes (also known as non-insulin-dependent diabetes mellitus, Type II diabetes) (9,10,11). Recent studies show that 85% of the individuals with Type II diabetes are obese (12).

Treatment of Diabetes. For many years, treatment was insulin therapy for Type I and oral sulfonylureas and/or insulin therapy for Type II. Metformin (glucophage) was the first antidiabetic drug approved by FDA (May 1995) for the treatment of Type II diabetes since the oral sulfonylureas were introduced in 1984. Metformin promotes the use of insulin already in the blood. This May 1995 approval was followed by the September 1995 approval of another antidiabetic drug, Acarbose (precose). It slows down the digestion and absorption of complex sugars, which reduces blood sugar levels after meals.

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Before 1982, insulin was purified from beef or pork pancreas. This was a problem for those diabetics allergic to animal insulin. Researchers produced a synthetic insulin called humulin. Approved by FDA in 1982, it was the first genetically engineered consumer health product manufactured for diabetics. Synthetic insulins can be produced in unlimited quantities.

Another possible treatment for diabetes includes surgically replacing the pancreas' endocrine tissues (islets of Langerhans) with healthy islet of Langerhans tissue grafts. Since 1988, 45 patients worldwide have undergone successful transplantation.

Complications. Complications of diabetes (end organ damage) include retinopathy, neuropathy, and nephropathy (traditionally designated as microvascular complications) as well as atherosclerosis (a macrovascular complication). Early stages of hyperglycemia can usually be controlled by an alteration in diet and increasing the amount of exercise, but drug treatment, including insulin, may be required. It has been shown that meticulous blood glucose control can

often slow down or halt the progression of diabetic complications if caught early enough (1). However, tight metabolic control is extremely difficult to achieve.

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Animal Models

Transgenic Mouse Models of Diabetes or Diabetes
Resistance. McGrane, et al., J. Biol. Chem. 263:11443-51
(1988) and Chen, et al., J. Biol. Chem., 269:15892-7 (1994)
describe the genetic engineering of mice to express bovine
growth hormone (bGH) or human growth hormone (hGH),
respectively. These mice exhibited an enhanced growth
phenotype. They also developed kidney lesions similar to
those seen in diabetic glomerulosclerosis, see Yang, et al.,
Lab. Invest., 68:62-70 (1993). Ogueta, et al., J.
Endocrinol., 165: 321-8 (2000) reported that transgenic mice
expressing bovine GH develop arthritic disorder and selfantibodies.

Growth hormone has many roles, ranging from regulation of protein, fat and carbohydrate metabolism to growth promotion. GH is produced in the somatrophic cells of the anterior pituitary and exerts its effects either through the GH-induced action of IGF-I, in the case of growth promotion, or by direct interaction with the GHR on target cells including liver, muscle, adipose, and kidney cells. Hyposecretion of GH during development leads to dwarfism, and hypersecretion before puberty leads to gigantism. adults, hypersecretion of GH results in acromegaly, a clinical condition characterized by enlarged facial bones, hands, feet, fatigue and an increase in weight. Of those individuals with acromegaly, 25% develop type II diabetes. This may be due to insulin resistance caused by the high circulating levels of GH leading to high circulating levels of insulin (Kopchick et al., Annual Rev. Nutrition 1999. 19:437-61).

A further mode of GH action may be through the transcriptional regulation of a number of genes contributing to the physiological effects of GH.

WO 2005/082398

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Growth hormone genes and the proteins encoded by them can be converted into growth hormone antagonists by mutation, see Kopchick USP 5,350,836. Transgenic mice have been made that express the GH antagonists bGH-G119R or hGH G120R, and which exhibit a dwarf phenotype. Chen, et al., J. Biol. Chem., 263:15892-7 (1994); Chen, et al., Mol. Endocrinol, 5:1845-52 (1991); Chen, et al., Proc. Nat. Acad. Sci. USA 87:5061-5 (1990). These mice did not develop kidney lesions. See Yang (1993), supra.

Chen, et al., Endocrinol, 136:660-7 (1995) compared the effect of streptozotocin treatment in normal nontransgenic mice, and in mice transgenic for (1) a GH receptor antagonist, the G119R mutant of bovine growth hormone or (2) the E117L-mutant of bGH. (According to Chen's ref. 24, these large GH transgenic streptozotocin-treated mice constitute an animal model for diabetes.) Glomerulosclerosis was seen in diabetic (STZ-treated) nontransgenic mice and in diabetic bGH-E117L mice, but not in diabetic bGH-G119R (GH antagonist) mice.

Two of the proteins which mediate growth hormone activity are the growth hormone receptor and the growth hormone binding protein, encoded by the same gene in mice(GHR/BP). It is possible to genetically engineer mice so that the gene encoding these proteins is disrupted ("knocked-out"; inactivated), see Zhou, et al., Proc. Nat. Acad. Sci. (USA), 94:13215-20 (1997). Zhou, et al. inactivated the GHR/BP gene by replacing the 3' portion of exon 4 (which encodes a portion of the GH binding domains) and the 5' region of intron 4 with a neomycin gene cassette. The modified gene was introduced into the target mice by homologous recombination. Like mice expressing a GH antagonist, homozygous GHR/BP-KO mice exhibit a dwarf phenotype. GHR/BP-KO mice, made diabetic by streptozotocin treatment, are protected from the development of diabetesassociated nephropathy. Bellush, et al., Endocrinol., 141:163-8 (2000).

High-Fat Diets. High-fat diets have been shown to induce both obesity and Type II diabetes in laboratory

PCT/US2005/005596 WO 2005/082398

animals (13). Surwit and colleagues demonstrated that male C57BL/6J mice are extremely sensitive to the diabetogenic effects of a high-fat diet when initiated at weaning. six months of age, high-fat fed animals had significantly elevated fasting blood-glucose and insulin levels and also demonstrated a decrease in insulin sensitivity (14). Ahren and colleagues (15) reported evidence of insulin resistance as well as diminished glucose-stimulated insulin release, after feeding with a high-fat diet for 12 weeks. These mice also showed elevated levels of total cholesterol, triglycerides, and free fatty acids, another hallmark of Type II diabetes.

15 Anatomy and Physiology of Muscle

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Muscle tissue constitutes about 40% of the body mass. Muscles may be classified by location, i.e., skeletal if attached to bone, cardiac if forming the wall of the heart, and visceral if associated with another body organ. may also be classified as voluntary or involuntary, depending on how their contractions and relaxations are controlled. Skeletal muscles are voluntary, while cardiac and visceral muscles are involuntary. It is also possible to classify muscles morphologically; skeletal and cardiac muscle cells are striated, whereas visceral muscle cells are not.

Each skeletal muscle is composed of many individual muscle cells called muscle fibers. The fibers are held together by fibrous connective-tissue membranes called fascia. fascium which envelops the entire muscle is the epimysium, and the fascia which penetrate the muscle, separating the fibers into bundles (fasciculi) are called perimysium. thin fascia (endomysium) sheath each muscle fiber. Skeletal muscles are attached either directly to a bone, or indirectly through a tendon.

The individual muscle fibers (cells) comprise threadlike protein structures called myofibrils.

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There are over 600 muscles in the human body. We will have occasion later to refer to the gastrocnemius. It is a superficial muscle in the posterior compartment of the lower leg, which together with the underlying soleus forms the characteristic bulge of the calf.

Role of Muscle in Development of Type II Diabetes

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Muscle, fat and liver tissues are the major contributors to the development of insulin resistance, hyperinsulinemia, and, ultimately, type II diabetes.

Muscle cells respond to insulin by increasing glucose uptake from the bloodstream. Muscle tissue can become resistant to insulin, causing the beta cells to initially increase insulin secretion. Eventually, though, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and they fail to respond to elevated blood glucose levels. Thus, clinical type 2 diabetes results from the combination of insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance. At least three steps-those mediated by glycogen synthase, hexokinase, and GLUT4-have been reported to be defective in patients with type 2 diabetes.

Fatty acids can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase. PKC-theata has also been implicated.

See generally Petersen, et al., "Pathogenesis of Skeletal muscle insulin resistance in type 2 diabetes mellitus", in "A Symposium: Evolution of type 2 diabetes mellitus management", at Amer. J. Cardiol., 90(5A): 11G-18G, (Sept. 5, 2002).

Adverse Effects of Type II Diabetes on Muscle

"Myopathy is a general term used to describe any disease of muscles, such as the muscular dystrophies and myopathies associated with thyroid disease. It can be caused

PCT/US2005/005596 WO 2005/082398

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by endocrine disorders, including diabetes, metabolic disorders, infection or inflammation of the muscle, certain drugs and mutations in genes. In diabetes, myopathy is thought to be caused by neuropathy, a complication of diabetes. General symptoms of myopathies include muscle weakness of limbs sometimes occurring during exercise although in some cases the symptoms diminish as exercise increases. Depending on the type of myopathy, one muscle group may be more affected than others." See "Joint and Muscle Problems Associated with Diabetes", www.iddtinternational.org/jointandmuscleproblems.html [Last modified June 12, 2003].

Diabetic muscle infarction can spontaneously affect patients with a long history of poorly controlled diabetes. "Most affected patients have multiple microvascular complications (neuropathy, nephropathy, and retinopathy). The clinical presentation is an acute onset of pain and swelling over days to weeks in the affected muscle groups (usually the thigh or calf), along with varying degrees of tenderness.... Therapy consists of rest and analgesia. Routine daily activities are not deleterious to the condition, but physical therapy may cause exacerbation. Spontaneous diabetic muscle infarction tends to resolve over a period of weeks to months in most cases." "Musculoskeletal Complications of Diabetes - Part 2", www.diabetic-lifestyle.com/articles/jan02 whats 1.htm [last modified Feb. 9, 2004]. See also Trujillo-Santos, et al., "Diabetes muscle infarction: an underdiagnosed complication of long-standing diabetes," Diabetes Care, 26(1):211-5 (2003).

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Identification of genes involved in hyperinsulinemia and type II diabetes, generally

Our attention recently has focused on the generation of muscle mRNA expression profiles and the identification of genes involved in the genesis of the obesity-induced hyperinsulinemia and type-II diabetes. To date, no one has attempted to study the actual progression from the normal condition to that of hyperinsulinemia or from hyperinsulinemia to Type II diabetes in an attempt to identify genes that are up-regulated or down-regulated in muscle as the disease progresses.

In previous studies aimed at identifying genes involved in diabetes-induced glomerulosclerosis, differential display and traditional subtractive hybridization techniques were used (16-20). While effective for the identification of a few genes (e.g. hmunc13, PED/PEA-15, lactate dehydrogenase, amiloride sensitive sodium channel, ubiquitin-like protein, mdr 1, and a-amyloid protein precursor as well as a few novel genes), these techniques can be quite labor intensive. The PCR-based method of subtractive hybridization requires less starting material, and allows the simultaneous isolation of all differentially expressed cDNAs into two groups (up-regulated and down-regulated).

However, the PCR-based method of subtractive hybridization is also quite labor-intensive, produced large numbers of false positive candidates and ultimately resulted in the identification of a relatively limited number of differentially expressed genes. (see Kelder1-USA application).

In order to expand the number of genes that can be analyzed simultaneously, several groups have begun to utilize DNA microarray analysis to measure differences in gene expression between normal and diseased states.

However, these experiments have been limited in regards to the number of experimental conditions analyzed. DNA microarray analysis has been performed on normal, obese and diabetic mice (21). Also, the obesity and diabetes in the

WO 2005/082398

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mouse models examined were caused by a specific endogenous genetic mutation (22). The differentially expressed genes in the above models may be very different from genes differentially expressed due to diet-induced obesity and Type-II diabetes.

The use of differential expression and related techniques to identify genes useful in the treatment of diabetes has been reviewed by Perfetti, et al., Diabetes Technol. & Therapeut., 5(3): 421-3 (2003). Bernal-Mizrachi, et al., Diabetes Metab. Res. Rev. 19: 32-42 (2003).

Other papers of interest include:

Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", Kidney Int, 59:1363-73 (2001);

Song, et al., "Cloning of a novel gene in the human kidney homologous to rat muncl3S: its potential role in diabetic nephropathy", Kidney Int., 53:1689-95 (1998);

' Page, et al., "Isolation of diabetes-associated kidney genes using differential display", Biochem. Biophys. Res. Comm., 232:49-53 (1997).

Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," Kidney Int. 53:926-31 (1998).

Condorelli, EMBO J., 17:3858-66 (1998).

Diabetes-Specific Differential Expression in Muscle Sreekumar, et al., "Gene expression profile in skeletal msucle of type 2 diabetes and the effect of insulin treatment," Diabetes 51: 1913 (June 2002) surveyed 6,451 genesw, and identified 85 genes for which there was an alteration in skeletal muscle transcription in diabetic patients after withdrawal of insulin treatment. Subsequent insulin treatment resulted in further changes in transcription of 74 of the 85 genes (15 increased, 59 decreased), and also resulted in alteration of 29 additional gene transcripts.

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Mootha, et al., "PCG-1\alpha responsive genes involved in oxidative phosphorylation are coordinatively downregulated in human diabetes," Nature Genetics 34(3); 267 (July 2003), used DNA microarrays to detect changes in the expression of sets of related genes, rather than of individual genes. They classified over 22,000 genes into 149 data sets; some of these data sets overlapped. They looked for a statistical correlation between the overall rank order of the genes in differential expression, and the groups to which the genes Expression was compared pairwise among three groups: males with normal glucose tolerance; males with impaired glucose tolerance; and males with type 2 diabetes. The set with the highest enrichment score (the one whose members ranked highly most often relative to chance expectation) was an internally curated set of 106 genes involved in oxidative phosphorylation. While the average decrease for the individual genes was modest (~20%), it was also consistent, being observed in 89% (94/106) of the genes in question. This paper is reviewed by Toye and Gauguier, "Genetics and functional genomics of type 2 diabetes mellitus", Genome Biology, 4: 241 (2003).

Patti, et al., "Coordinated reduction of genes of oxidative metabolism in humans with insulin resistance and diabetes: Potential role of PGC1 and NRF1", Proc. Nat. Acad. SCi. (USA), 100(14): 8466 (July 8, 2003) used microarrays to analyze skeletal muscle expression of genes in nondiabetic insulin-resistant subjects at high risk for diabetes (based on family hisotry of diabetes and Mexican-American ethnicity) and diabetic Mexican-American subjects. Of 7,129 sequences represented on the microarray, 187 were differentially expressed between control and diabetic However, no single gene remained significantly differentially expressed after controlling for multiple comparison false discovery by using the Benjamini-Hochberg method, see Benjamini, et al., J. R. Stat. Soc. Sert. B. 57:289-300 (1995); Dudait, et al., Stat. Sin. 12: 111-139 Consequently, Patti et al. sought to identify (2002).

groups of related genes with similar patterns of differential expression using MAPP FINDER and ONTOEXPRESS. According to MAPP FINDER, the top-ranked cellular component terms were mitochondrion, mitochondrial membrane, mitochondrial inner membrane, and ribosome, and the topranked process term was ATP biosynthesis. According to ONTOEXPRESS, the over-represented groups were energy generation, protein biosynthesis/ribosomal proteins, RNA binding, ribosomal structural protein, and ATP synthase complex.

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Huang, Xudong, "Identification of abnormally expressed genes in skeletal muscle contributing to insulin resistance and type 2 diabetes", Thesis, document id: 9576 Lunds University 2002, reported differential expression of the mitochondrially-encoded ND1 gene in human diabetic patients and of the nuclear-encoded cathepsin L gene in mice.

Standaert, et al., ": Skeletal muscle insulin resistance in obesity-associated type 2 diabetes in monkeys is linked to a defect in insulin activation of protein kinase Czeta/lambda/iota Diabetes 51: 2936 (Oct. 2002). the authors concluded that defective activation of atypical PKCs played an important role in the patchogenesis of peripheral insulin resistance in both obese prediabetic and diabetic monkeys. They attributed this linkage to the apparent requirement for aPKCs during insulin-stimulated glucose transport.

Srommer, et al., Am. J. Physiol., "Skeletal muscle insuling resistance after trauma: insulin signaling and glucose transport", 275(2 Pt. 1): E3518(Aug. 1998) concluded that insulin resistance in skeletal muscle after surgical trauma is associated with reduced glucose transport but not with impaired glucose signaling to PI 3-kinase or its downstream target, Akt.

Aging-Specific Differential Expression in Muscle

WO 2005/082398

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Gene Chip-Based Identification of genes involved in aging of skeletal muscle

Several groups have used DNA microarrays to measure differences in gene expression caused by the aging process. However, these experiments are extremely limited in regards to the number of aging time points or experimental conditions.

Weindruch, et al., "Microarray profiling of gene expression in aging and its alteration by caloric restriction in mice" in Symposium: Calorie Restriction: effects on Body Composition, Insulin Signaling and Aging 918S-923S (2001) (21) compared expression in gastrocnemius muscle from 5- and 30-month old C57BL/6 mice, with and without caloric restriction. In this analysis, the expression of 113 genes was found to be changed by at least two-fold in 5-month old mice compared to 30-month old mice. Caloric restriction of comparable mice caused a reversal of the altered gene expression of 33 genes.

Of the 6347 genes surveyed in the oligonucleotide microarray, only 58 (0.9%) displayed a greater than 2 fold increase in gene expression as a function of aging, whereas 55(0.9%) displayed a greater than 2 fold decrease.

Of the genes positively correlated with aging, 16% could be assigned to stress responses. The largest differential expression between young and aged animals (3.8 fold) was the mitochondrial sarcomeric creatine kinase.

Of the genes negatively correlated with aging, 13% were involved in energy metabolism. A noteworthy number were genes encoding biosynthetic enzymes (cytochrome P450 IIC12, squaelene synthase, stearoyl-CoA desaturase, EF-1-gamma. Another down regulator was a CpG binding protein, MeCP2.

Weindruch further reported that age-related changes in gene expression profile were "remarkably attenuated" by caloric restriction.

What appears to be the same experiment is discussed in Lee, et al., "Gene expression profile of aging and its retardation by caloric restriction," Science, 285: 1390 (Aug. 27, 1999). This papers lists the individual genes which

were differentially expressed by more than 2-fold, and classifies them as energy metabolism, neuronal factors, protein metabolism, stress response, biosynthesis, calcium metabolism or DNA repair genes.

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Welle, et al., "Skeletal muscle gene expression profiles in 20-29 year old and 65-71 year old women," Exper. Gerontol., 39: 369-77 (2004) and available electronically as doi:10.1016/j.exger.2003.11.011 studied gene expression and physical condition in seven young and eight older women. With respect to physical condition, the measured or calculated parameters were total body mass, lean body mass, left leg lean mass (by biopsy), maximum isometric left knee extension force, left knee extension force/left keg lean mass, Peak VO2/lean body mass, and Peak VO2/left leg lean mass.

There were 1178 "probe sets" (representing 1053 different Unique clusters) for which differential expression was detected; 550 for which expression was higher in older women, and 628 the inverse effect. The differences ranged from 1.2 to 4 fold; most (78A%) were less than 1.5 fold. The complete list of differentially expressed genes is given in the Rochester Muscle database website, www.urmc.rochester.edu/smd/crc/swindex (".html" omitted, in accordance with USPTO requirements, so that the publication of this application will not create an active hyperlink).

The gene most highly overexpressed in older muscle was p21 (cyclin-dependent kinase inhibitor 1A) (4.01 fold). This one of several genes (see Welle Table 2) which are potentially related to DNA damage and repair. Welle also thought it noteworthy how many of the differentially expressed genes were ones that encode proteins which bind to pre-mRNAs or mRNAs (see Welle Table 3).

Other Differential/Subtractive Hybridization Studies of Interest

Zhang, et al., Kidney International, 56:549-558 (1999) identified genes up-regulated in 5/6 nephrectomized

PCT/US2005/005596 WO 2005/082398

(subtotal renal ablation) mouse kidney by a PCR-based subtraction method. Ten known and nine novel genes were The ultimate goal was to identify genes involved in glomerular hyperfiltration and hypertrophy. Melia, et al., Endocrinol., 139:688-95 (1998) applied subtractive hybridization methods for the identification of androgen-regulated genes in mouse kidney. The treatment mice were dosed with dihydrotestosterone, an androgen. Kidney androgen-regulated protein gene was used as a positive control, as it is known to be up-regulated by DHT.

See also Holland, et al., Abstract 607, "Identification of Genes Possibly Involved in Nephropathy of Bovine Growth Hormone Transgenic Mice" (Endocrine Society Meeting, June 22, 2000) and Coschigano, et al., Abstract 333, "Identification of Genes Potentially Involved in Kidney Protection During Diabetes" (Endocrine Society Meeting, June 22, 2000).

The following differential hybridization articles may also be of interest: Wada, et al., "Gene expression profile in streptozotocin-induced diabetic mice kidneys undergoing glomerulosclerosis", Kidney Int, 59:1363-73 (2001); Song, et al., "Cloning of a novel gene in the human kidney homologous to rat muncl3S: its potential role in diabetic nephropathy", Kidney Int., 53:1689-95 (1998); Page, et al., "Isolation of diabetes-associated kidney genes using differential display", Biochem. Biophys. Res. Comm., 232:49-53 (1997); Peradi, "Subtractive hybridization claims: An efficient technique to detect overexpressed mRNAs in diabetic nephropathy," Kidney Int. 53:926-31 (1998); Condorelli, EMBO J., 17:3858-66 (1998).

Apoptosis and CIDE-A

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Apoptosis is a form of programmed cell death that occurs in an active and controlled manner to eliminate unwanted cells. Apoptotic cells undergo an orchestrated cascade of morphological changes such as membrane blebbing,

often leads to tissue inflammation.

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nuclear shrinkage, chromatin condensation, and formation of apoptotic bodies which then undergo phagocytosis by neighboring cells. One of the hallmarks of cellular apoptosis is the cleavage of chromosomal DNA into discrete oligonucleosomal size fragments. This orderly removal of unwanted cells mirnimizes the release of cellular components that may affect neighboring tissue. In contrast, membrane rupture and release of cellular components during necrosis

The process of apoptosis is highly conserved and involves the activation of the caspase cascade. Cohen, GM. (1997) Caspases: the executioners of apoptosis. Biochem. J. 326:1-16; Budihardjo, I., Oliver, H., Lutter, M., Luo, X., Wang, X. (1999) Biochemical pathways of caspase activation during apoptosis. Annnu. Rev. Cell. Dev. Biol.15:269-290; Jacobson, M.D., Weil, M., Raff, M.C. (1997) Programmed cell death in animal development. Cell 88:347-354. Caspases are a family of serine proteases that are synthesized as inactive proenzymes. Their activation by 20 apoptotic signals such as CD95 (Fas) death receptor activation or tumor necrosis factor results in the cleavage of specific target proteins and execution of the apoptotic program. Apoptosis may occur by either an extrinsic pathway involving the activation of cell surface death receptors (DR) or by an intrinsic mitochondrial pathway. Yoon, J-H. Gores G.J. (2002) Death receptor-mediated apoptosis and : the liver. J. Hepatology 37:400-410.

These pathways are not mutually exclusive and some cell types require the activation of both pathways for maximal apoptotic signaling. In type-I cells, death receptor activation leads to the recruitment and activation of caspases-8/10 and the rapid cleavage and activation of caspase-3 in a mit ochondrial-independent manner. Hepatocytes are members of the Type-II cells in which mitochondria are essential for DR-mediated apoptosis Scaffidi, C., Fulda, S., Srinivasan, A., Friesen, C., Li, F., Tomaselli, K.J., Debatin, K.M., Krammer, P.H., Peter, M.E. (1998) Two CD95 (APO-1/Fas) signaling pathways. 17:1675-1687. In this pathway, the pro-apoptotic protein

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Bid is truncated by activated caspases-8/10 and translocates to the mitochondria. Luo, X., Budihardjo, I., Zou, H., Slaughter, C., Wang, X. (1998) Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. Cell 94:481-490; Li, H., Zhu, H., Xu, C.J., Yuan, J. (1998) Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis. Cell 94:491-501. This translocation leads to mitochondrial cytochrome c release and eventual activation of caspases-3 and 7 via cleavage by activated caspase-9.

One of the substrates for activated caspase-3 is the DNA fragmentation factor (DFF). DFF is composed of a 45 kDa regulatory subunit (DFF45) and a 40 kDA catalytic subunit (DFF40). Liu, X., Zou, H., Slaughter, C., Wang, DFF, a heterodimeric protein that functions downstream of caspase-3 to trigger DNA fragmentation during apoptosis. Cell 89:175-184. DFF45 cleavage by activated caspase-3 results in its dissociation from DFF40 and allows the caspase-activated DNAse (CAD) activity of DFF40 to cleave chromosomal DNA into oligonucleosomal size fragments. Liu, X., Li, P., Widlak, P., Zou, H., Luo, X., Garrard, W.T., Wang, X. (1998) The 40-kDa subunit of DNA fragmentation factor induces DNA fragmentation and chromatin condensation during apoptosis. Proc. Natl. Acad. Sci. USA. 95:8461-8466; Halenbeck, R., MacDonald, H., Roulston, A., Chen, T.T., Conroy, L., Williams, L.T. (1998) CPAN, a human nuclease regulated by the caspase-sensitive inhibitor Curr Biol. 8:537-540; Nagata, S. (2000) Apoptotic DFF45. DNA fragmentation. Exp. Cell Res. 256:12-8.

Recently, a novel family of cell-death-inducing DFF45-like effectors (CIDEs) have been identified that includes CIDE-A, CIDE-B and CIDE-3/FSP2. Inohara, N., Koseki, T., Chen, S., Wu, X., Nunez, G. (1998) CIDE, a novel family of cell death activators with homology to the 45 kDa subunit of the DNA fragmentation factor. EMBO J. 17:2526-2533; Danesch, U., Hoeck, W., Ringold, G.M. (1992) Cloning and transcriptional regulation of a novel adipocyte-specific gene, FSP27. CAAT-enhancer-binding protein (C/EBP)

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and C/EBP-like proteins interact with sequences required for differentiation-dependent expression. J. Biol. Chem. 267:7185-7193; Liang, L., Zhao, M., Xu, Z., Yokoyama, K.K., Li, T. (2003) Molecular cloning and characterization of CIDE-3, a novel member of the cell-death-inducing DNA-fragmentation-factor (DFF45)-like effector family. Biochem. J. 370:195-203.

The CIDEs contain an N-terminal domain that shares homology with the N-terminal region of DFF45 and may represent a regulatory region via protein interaction. See Inohara, supra; Lugovskoy, A.A., Zhou, P., Chou, J.J., McCarty, J.S., Li, P., Wagner, G. (1999) Solution structure of the CIDE-N domain of CIDE-B and a model for CIDE-N/CIDE-N interactions in the DNA fragmentation pathway of apoptosis. Cell 9:747-755. The family members also share a C-terminal domain that is necessary and sufficient for inducing cell death and DNA fragmentation; see Inohara supra. The overexpression of CIDE-A induces cell death that can be inhibited by DFF45. However, CIDE-A-induced apoptosis is not inhibited by caspase-8 inhibitors thereby suggesting the presence of additional, caspase-independent, pathway(s) for the induction of apoptosis, see Inohara supra. Previous reports have indicated that human and mouse CIDE-A are expressed in several tissues such as brown adipose tissue (BAT) and heart and are localized to the mitochondria, Zhou, Z., Yon Toh, S., Chen, Z., Guo, K., Ng, C.P., Ponniah, S., Lin, S.C., Hong, W., Li, P. (2003) Cidea-deficient mice have lean phenotype and are resistant to obesity. Nat. Genet. 35:49-56. . In addition to the ability to induce apoptosis, CIDE-A can interact and inhibit. UCP1 in BAT and may therefore play a role in regulating energy balance, see Zhou supra.

Previous reports have indicated that CIDE-A is not expressed in either adult human or mouse liver tissue, see Inohara supra, Zhou supra.

The human protein cell death activator CIDE-A is of particular interest because of its highly dramatic change in liver expression with age, first demonstrated in our

Kopchick7 application, supra. CIDE-A expression is elevated in older normal mice. CIDE-A expression was studied for normal C57BI/6J mouse ages 35, 49, 77, 133, 207, 403 and 558 days. Expression is low at the first five data points, then rises sharply at 403 days, and again at 558 days.

CIDE-A was therefore classified as an "unfavorable protein", i.e., it was taught that an antagonist to CIDE-A could retard biological aging.

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In Kopchick7A-PCT we reported that CIDE-A is also prematurely expressed in hyperinsulinemic and type-II diabetic mouse liver tissue. CIDE-A expression also correlates with liver steatosis in diet-induced obesity, hyperinsulinemia and type-II diabetes. These observations suggest an additional pathway of apoptotic cell death in Non-Alcoholic Fatty Liver Disease (NAFLD) and that CIDE-A may play a role in this serious disease and potentially in liver dysfunction associated with type-II diabetes.

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Differential hybridization techniques have been used to identify mouse genes that are differentially expressed in the muscle (gastrocnemius) of mice, depending upon their

development of hyperinsulinemia or type II diabetes.

In essence, complementary RNA derived from normal mice, or mouse models of hyperinsulinemia or type II diabetes, was screened for hybridization with oligonucleotide probes each specific to a particular mouse database DNA, the latter being identified, by database accession number, by the gene manufacturer. Each database DNA in turn was also identified by the gene chip manufacturer as representative of a particular mouse gene cluster (Unigene).

In most cases, this database DNA sequence is a full length genomic DNA or cDNA sequence, and is therefore either identical to, or otherwise encodes the same protein as does, a natural full-length genomic DNA protein coding sequence. Those which don't present at least a partial sequence of a natural gene or its cDNA equivalent.

For the sake of simplicity, all of these mouse database DNA sequences, whether full-length or partial, and whether cDNA or genomic DNA, are referred to herein as "mouse genes". When only the genomic sequence is intended, we will refer specifically to "genomic DNA" or "gDNA".

The sequences in the protein databases are determined either by directly sequencing the protein or, more commonly, by sequencing a DNA, and then determining the translated amino acid sequence in accordance with the Genetic Code. All of the mouse sequences in the mouse polypeptide database are referred to herein as "mouse proteins" regardless of whether they are in fact full length sequences.

Mouse genes which were differentially expressed (normal vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or normal vs. diabetic), as measured by different levels of hybridization of the respective cRNA samples with the particular probe corresponding to that mouse gene) were identified.

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Since the progression is from normal to hyperinsulinemic, and thence from hyperinsulinemic to type II diabetic, one may define mammalian subjects as being more favored or less favored, with normal subjects being more favored than hyperinsulinemic subjects, and hyperinsulinemic subjects being more favored than type II diabetic subjects. The subjects' state may then be correlated with their gene expression activity.

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The terms "normal" and "control" are used interchangeably in this specification, unless expressly stated otherwise. The control or normal subject is a mouse which is normal vis-a-vis fasting insulin and fasting glucose levels. The term "normal", as used herein, means normal relative to those parameters, and does not necessitate that the mouse be normal in every respect.

A mouse gene is said to have exhibited a favorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is higher than that in mice which are in a less favored state. A mouse gene is said to have exhibited an unfavorable behavior if, for a particular mouse age of observation, its average level of expression in mice which are in a more favored state is lower than that in mice which are in a less favored state.

When we observe the mice at several different ages, it is possible for their expression behavior to vary from time point to time point. For a given comparison of subjects, e.g., normal vs. hyperinsulinemic, we classify the mouse gene as favorable or unfavorable on the basis of the direction of the largest expression change, and it is the magnitude of this largest expression change, expressed as a ratio of greater to lesser, which is set forth in the Master Table 1 data for that mouse gene. Thus, if at 2 weeks, there was a 3-fold favorable behavior, and at 8 weeks, there was a 4-fold unfavorable behavior, and at all other observed time points, the behavior was weaker than 3-fold, the mouse gene would be classified as an unfavorable gene with respect to the subject comparison in question.

WO 2005/082398

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It will be appreciated that it may be that if the mouse gene were observed at an age other than one of the ages noted in the Examples, we would have observed a still stronger differential expression behavior. Nonetheless, we must classify the mouse genes on the basis of the behavior which we actually observed, not the behavior which might have been observed at some other age.

We are particularly interested in mouse genes which exhibit strongly favorable or unfavorable differential expression behaviors. A behavior is considered strong if the ratio of the higher level to the lower level is at least two-fold.

However, a mouse gene may still be identified as favorable or unfavorable even if none of its observed behaviors are strong as defined above. In general, we consider the consistency of its behaviors (that is, are all or most of the differential expression behaviors at different ages in the same direction, e.g., hyperinsulinemic higher than control), the magnitude of the behaviors (higher the better), and the expression behavior of structurally or functionally related mouse genes (a mouse gene is more likely to be identified as favorable on the basis of a weakly favorable behavior if it is related to other mouse genes which exhibited favorable, especially strongly favorable, behavior). If we considered a mouse gene with only weak differential expression behavior to be worthy of consideration on the basis of these criteria, then we listed it in Master Table 1 in the appropriate subtable.

Preferably, the differential behavior observed is both strong and consistent. Preferably, if related mouse genes were tested, they exhibit the same direction of differential expression behavior.

A mouse gene which was more strongly expressed in hyperinsulinemic tissue than in either normal or type II diabetic tissue (i.e., C<HI, HI>D) will be deemed both "unfavorable", by virtue of the control:hyperinsulinemic comparison, and "favorable", by virtue of the

hyperinsulinemic:diabetic comparison. This is one of several possible "mixed" expression patterns.

Thus, we can subdivide the "favorables" into wholly and partially favorables. Likewise, we can subdivide the unfavorables into wholly and partially unfavorables. The genes/proteins with "mixed" expression patterns are, by definition, both partially favorable and partially unfavorable. In general, use of the wholly favorable or wholly unfavorable genes/proteins is preferred to use of the partially favorable or partially unfavorable ones.

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It is evident from the foregoing that mixed genes/proteins are those exhibiting a combination of favorable and unfavorable behavior. A mixed gene/protein can be used as would a favorable gene/protein if its favorable behavior outweighs the unfavorable. It can be used as would an unfavorable gene/protein if its unfavorable behavior outweighs the favorable. Preferably, they are used in conjunction with other agents that affect their balance of favorable and unfavorable behavior. Use of mixed genes/proteins is, in general, less desirable than use of purely favorable or purely unfavorable genes/proteins, but it is not excluded.

It should be noted that a mouse gene is classified on the basis of the strongest C-HI behavior among the ages tested, the strongest HI-D behavior among the ages tested, and the strongest C-D behavior among the ages tested. If at least one of these three behaviors is significantly favorable, and none of the others of these three behaviors is significantly unfavorable, the mouse gene will be classified as wholly favorable and listed in subtable IA of Master Table 1. However, that does not mean that it may not have exhibited a weaker but unfavorable expression behavior at some tested age.

The "favorable", "unfavorable" and "mixed" mouse proteins of the present invention include the mouse database proteins listed in the Master Table in the same row as a particular "favorable", "unfavorable" or "mixed" mouse gene, respectively. These proteins may be the exact translation product of the identified mouse gene (database DNA).

However, if they were sequenced directly, they could be shorter or longer than that translation product. They could also differ in sequence from the exact translation product as a result of post-translational modifications.

The mouse proteins of interest also include mouse proteins which, while not listed in the table, correspond to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) such mouse proteins or genes, and mouse proteins which are at least substantially identical or conservatively identical to the listed mouse proteins.

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Related human genes (database DNAs) and proteins were identified by searching a database comprising human DNAs or proteins for sequences corresponding to (i.e., homologous to, i.e., which could be aligned in a statistically significant manner to) the mouse gene or protein. More than one human protein may be identified as corresponding to a particular mouse chip probe and to a particular mouse gene.

Note that the terms "human genes" and "human proteins" are used in a manner analogous to that already discussed in the case of "mouse genes" and "mouse proteins".

As used herein, the term "corresponding" does not mean identical, but rather implies the existence of a statistically significant sequence similarity, such as one sufficient to qualify the human protein or gene as a homologus protein or DNA as defined below. The greater the degree of relationship as thus defined (i.e., by the statistical significance of each alignment used to connect the mouse cDNA to the human protein or gene, measured by an E value), the more close the correspondence. The connection may be direct (mouse gene to human protein) or indirect (e.g., mouse gene to human gene, human gene to human protein). By "mouse gene", we mean the mouse gene from which the gene chip DNA in question was derived.

In general, the human genes/proteins which most closely correspond, directly or indirectly, to the mouse genes are preferred, such as the one(s) with the highest, top two

highest, top three highest, top four highest, top five highest, and top ten highest E values for the final alignment in the connection process. The human genes/proteins deemed to correspond to our mouse genes are identified in the Master Tables.

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Note that it is possible to identify homologous fulllength human genes and proteins, if they are present in the database, even if the query mouse DNA or protein sequence is not a full-length sequence.

If there is no homologous full-length human gene or protein in the database, but there is a partial one, the latter may nonetheless be useful. For example, a partial protein may still have biological activity, and a molecule which binds the partial protein may also bind the full-length protein so as to antagonize a biological activity of the full-length protein. Likewise, a partial human gene may encode a partial protein which has biological activity, or the gene may be useful in the design of a hybridization probe or in the design of a therapeutic antisense DNA.

The partial genes and protein sequences may of course also be used in the design of probes intended to identify the full length gene or protein sequence.

For the sake of convenience, we refer to a human protein as favorable if (1) it is listed in Master Table 1 as corresponding to a favorable mouse gene, or (2) it is at least substantially identical or conservatively identical to a listed protein per (1), or (3) it is a member of a human protein class listed in Master Table 2 (if provided) as corresponding to a favorable mouse gene. We define a human protein as unfavorable in an analogous manner. We may further identify a human protein as being wholly favorable (see mouse genes of subtable 1A, wholly unfavorable (see mouse genes of subtable 1B), or mixed, i.e., both partially favorable and partially unfavorable (see mouse genes of subtable 1C).

Likewise, a human gene which encodes a particular human protein may be classified in the same way as the human protein which it encodes.

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However, it should be noted that this classification is not based on the direct study of the expression of the human gene/protein. of course, the human genes/proteins of ultimate interest will be the ones whose change in level of expression is, in fact, correlated, directly or inversely, with the change of state (normal, hyperinsulinemic, diabetic) of the subject.

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After identifying related human genes and proteins, one may formulate agents useful in screening humans at risk for progression toward hyperinsulinemia or toward type II diabetes, or protecting humans at risk thereof from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

Agents which bind the "favorable" and "unfavorable" nucleic acids (e.g., the agent is a substantially complementary nucleic acid hybridization probe), or the corresponding proteins (e.g., an antibody vs. the protein) may be used to evaluate whether a human subject is at increased or decreased risk for progression toward type II A subject with one or more elevated "unfavorable" and/or one or more depressed "favorable" genes/proteins is at increased risk, and one with one or more elevated "favorable" and/or one or more depressed "unfavorable" genes/proteins is at decreased risk. One may further take into account whether the subject is normoinsulinemic or hyperinsulinemic at the time of the assay. is non-diabetic and normoinsulinemic, we are especially . interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in hyperinsulinemic vs. normal muscle. If the subject is already hyperinsulinemic, yet non-diabetic, we are especially interested in the "favorable" and "unfavorable" human genes/proteins corresponding to mouse genes differentially expressed in type II diabetic vs. hyperinsulinemic muscle.

The assay may be used as a preliminary screening assay to select subjects for further analysis, or as a formal diagnostic assay.

The identification of the related genes and proteins may also be useful in protecting humans against these disorders.

Thus, Applicants contemplate:

WO 2005/082398

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- (1) use of the "favorable" mouse DNAs (or fragments thereof) of the Master Tables (below) to isolate or identify related human DNAs;
 - (2) use of human DNAs, related to favorable mouse DNAs, to express the corresponding human proteins;
- (3) use of the corresponding human proteins (and mouse proteins, if biologically active in humans), to protect against the disorder(s);
- (4) use of the corresponding mouse or human proteins, or nucleic acid probes derived from the mouse or human genes, in diagnostic agents, in assays to measure progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage; and
- (5) use of the corresponding human or mouse genes therapeutically in gene therapy, to protect against the disorder(s).

Moreover Applicants contemplate:

- (1) use of the "unfavorable" mouse DNAs (or fragments thereof) of the Master Tables to isolate or identify related human DNAs;
- (2) use of the complement to the "unfavorable" mouse DNAs or related human DNAs, as antisense molecules to inhibit expression of the related human DNAs;
- (3) use of the mouse or human DNAs to express the corresponding mouse or human proteins;
- (4) use of the corresponding mouse or human proteins, in diagnostic agents, to measure progression toward hyperinsulinemia or type II diabetes, or protection against the disorder(s), or to estimate related end organ damage such as kidney damage;

(5) use of the corresponding mouse or human proteins in assays to determine whether a substance binds to (and hence may neutralize) the protein; and

(6) use of the neutralizing substance to protect against the disorder(s).

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Thus, DNAs of interest include those which specifically hybridize to the aforementioned mouse or human genes, and are thus of interest as hybridization assay reagents or for antisense therapy. They also include synthetic DNA sequences which encode the same polypeptide as is encoded by the database DNA, and thus are useful for producing the polypeptide in cell culture or in situ (i.e., gene therapy). Moreover, they include DNA sequences which encode polypeptides which are substantially structurally identical or conservatively identical in amino acid sequence to the mouse and human proteins identified in the Master Table 1, subtables 1A or 1C. Finally, they include DNA sequences which encode peptide (including antibody) antagonists of the proteins of Master Table 1, subtables 1B or 1C.

The related human DNAs may be identified by comparing the mouse sequence (or its AA translation product) to known human DNAs (and their AA translation products).

Related human DNAs also may be identified by screening human cDNA or genomic DNA libraries using the mouse gene of the Master Table, or a fragment thereof, as a probe.

If the mouse gene of Master Table 1 is not full-length, and there is no closely corresponding full-length mouse gene in the sequence databank, then the mouse DNA may first be used as a hybridization probe to screen a mouse cDNA library to isolate the corresponding full-length sequence.

Alternatively, the mouse DNA may be used as a probe to screen a mouse genomic DNA library.

Our animal models of hyperinsulinemia and diabetes are also obese. It is possible that the genes found to be favorable act indirectly by inhibiting obesity. Likewise, it is possible that the genes found to be unfavorable act indirectly by accentuating obesity. Consequently, it is

within the compass of the present invention to use the favorable genes and proteins, or to use antagonists of the unfavorable genes and proteins, to protect against obesity, as well as against sequelae of obesity such as hyperinsulinemia and diabetes.

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Since type II diabetes is an age-related disease, the agents of the present invention may be used in conunction with known anti-aging or anti-age-related disease agents. It is of particular interest to use the agents of the present invention in conjunction with an agent disclosed in one of the related applications cited above, in particular, an antagonist to CIDE-A, the latter having been taught in Kopchick7 and Kopchick7A-PCT.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Body weight gain [Fig. 1a], fasting glucose [Fig. 1b] and fasting insulin [Fig. 1c] levels of mice on the HF or Std diets.

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Figure 2. Expression levels of Actin, alpha, cardiac (Actc1, NM_009608) using RNA isolated from gastrocnemius muscle of individual diabetic HF mice and corresponding Std mice at different time points.

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Figure 3. Data shown are expression levels for additional actin-related and actin-binding genes exhibiting a consistent decrease in expression in the HF mice in comparison to Std mice at all four time points (Fig. 3(a)) or at three of the four time points (Fig. 3(b)).

WO 2005/082398

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS OF THE INVENTION

Full-Length vs. Partial Length Genes/Proteins

A "full length" gene is here defined as (1) a naturally occurring DNA sequence which begins with an initiation codon (almost always the Met codon, ATG), and ends with a stop codon in phase with said initiation codon (when introns, if any, are ignored), and thereby encodes a naturally occurring polypeptide with biological activity, or a naturally occurring precursor thereof, or (2) a synthetic DNA sequence which encodes the same polypeptide as that which is encoded by (1). The gene may, but need not, include introns.

A "full-length" protein is here defined as a naturally occurring protein encoded by a full-length gene, or a protein derived naturally by post-translational modification of such a protein. Thus, it includes mature proteins, proproteins, preproteins and preproproteins. It also includes substitution and extension mutants of such naturally occurring proteins.

Subjects

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A mouse is considered to be a diabetic subject if, regardless of its fasting plasma insulin level, it has a fasting plasma glucose level of at least 190 mg/dL. A mouse is considered to be a hyperinsulinemic subject if its fasting plasma insulin level is at least 0.67 ng/mL and it does not qualify as a diabetic subject. A mouse is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

A mouse is considered "obese" if its weight is at least 15% in excess of the mean weight for mice of its age and sex. A mouse which does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

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WO 2005/082398

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A human is considered a diabetic subject if, regardless of his or her fasting plasma insulin level, the fasting plasma glucose level is at least 126 mg/dL. A human is considered a hyperinsulinemic subject if the fasting plasma insulin level is more than 26 micro International Units/mL (it is believed that this is equivalent to 1.08 ng/mL), and does not qualify as a diabetic subject. A human is considered to be "normal" if it is neither diabetic nor hyperinsulinemic. Thus, normality is defined in a very limited manner.

A human is considered "obese" if the body mass index (BMI) (weight divided by height squared) is at least 30 kg/m². A human who does not satisfy this standard may be characterized as "non-obese", the term "normal" being reserved for use in reference to glucose and insulin levels as previously described.

A human is considered overweight if the BMI is at least 25 kg/m². Thus, we define overweight to include obese individuals, consistent with the recommendations of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). A human who does not satisfy this standard may be characterized as "non-overweight."

According to the Report of the Expert Committe on the Diagnosis and Classification of Diabetes Mellitus, Diabetes Care 20: 1183-97 (1997), the following are risk factors for diabetes type II:

older (e.g., at least 45; see below)

excessive weight (see below)

first-degree relative with diabetes mellitus

member of high risk ethnic group (black, Hispanic, Native American, Asian)

history of gestational diabetes mellitus or delivering a baby weighing more than 9 pounds (4.032 kg)

hypertensive (>140/90 mm Hg)

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HDL cholesterol level >35 mg/dL (0.90 mmol/L)

triglyceride level >=250 mg/dL (2.83 mmol/L)

Hence, in a preferred embodiment, the diagnostic and protective methods of the present invention are applied to human subjects exhibiting one or more of the aforementioned risk factors. Likewise, in a preferred embodiment, they are applied to human subjects who, while not diabetic, exhibit impaired glucose homeostasis (110 to <126 mg/dL).

The risk of diabetes increases with age. Hence, in successive preferred embodiments, the age of the subjects is at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, and at least 75.

With regard to excessive weight, NEDDK says that "The relative risk of diabetes increases by approximately 25 percent for each additional unit of BMI over 22." Hence, in successive preferred embodiments, the BMIs of the human subjects is at least 23, at least 24, at least 25 (i.e., overweight by our criterion), at least 26, at least 27, at least 28, at least 29, at least 30 (i.e., obese), at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at least 38, at least 39, at least 40, or over 40.

Age-Related Diseases

Age-related (senescent) diseases include certain cancers, atherosclerosis, diabetes (type 2), osteoporosis, hypertension, depression, Alzheimer's, Pærkinson's, glaucoma, certain immune system defects, kidney failure, and liver steatosis. In general, they are diseases for which the relative risk (comparing a subpopulation over age 55 to a suitably matched population under age 55) is at least 1.1.

Preferably, the agents of the present invention protect against one or more age-related diseases for at least a subpopulation of mature (post-puberty) adult subjects.

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Direct and Indirect Utility of Identified Nucleic Acid Sequences and Related Molecules

The mouse or human genes (or fragments thereof) may be used directly. For diagnostic or screening purposes, they (or specific binding fragments thereof) may be labeled and used as hybridization probes. For therapeutic purposes, they (or specific binding fragments thereof) may be used as antisense reagents to inhibit the expression of the corresponding gene, or of a sufficiently homologous gene of another species.

If the database DNA appears to be a full-length cDNA or gDNA, that is, it encodes an entire, functional, naturally occurring protein, then it may be used in the expression of that protein. Likewise, if the corresponding human gene is known in full-length, it may be used to express the human protein. Such expression may be in cell culture, with the protein subsequently isolated and administered exogenously to subjects who would benefit therefrom, or in vivo, i.e., administration by gene therapy. Naturally, any DNA encoding the same protein may be used for the same purpose, and a DNA encoding a protein which a fragment or a mutant of that naturally occurring protein which retains the desired activity, may be used for the purpose of producing the active fragment or mutant. The encoded protein of course has utility therapeutically and, in labeled or immobilized form, diagnostically.

The genes may also be used indirectly, that is, to identify other useful DNAs, proteins, or other molecules. We have attempted to determine whether the mouse genes disclosed herein have significant similarity to any known human DNA, and whether, in any of the six possible combinations of reference frame and strand, they encode a protein similar to a known human protein. If so, then it

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follows that the known human protein, and DNAs encoding that protein, may be used in a similar manner. In addition, if the known human protein is known to have additional homologues, then those homologous proteins, and DNAs encoding them, may be used in a similar marner.

There thus are several ways that a human protein homologue of interest can be identified by database searching, including but not limited to:

- 1) a DNA->DNA (BlastN) search for human database DNAs closely related to the mouse gene identifies a known human gene, and the sequence of the human protein is deduced by the Genetic Code;
- 2) a DNA->Protein (BlastX) search for humn database proteins closely related to the translated DNA of the mouse gene identifies a known human protein; and
- 3) the sequence of the mouse protein is known or is deduced by the Genetic Code, and a Protein->Protein (BlastP) search for closely related database proteins identifies a known human protein.

Once a known human gene is identified, it may be used in further BlastN or BlastX searches to identify other human genes or proteins. Once a known human protein is identified, it may be used in further BlastP searches to identify other human proteins.

Searches may also take cognizance, intermediately, of known genes and proteins other than mouse or human ones, e.g., use the mouse sequence to identify a known rat sequence and then the rat sequence to identify a human one.

If we have identified a mouse gene, and it encodes a mouse protein which appears similar to a human protein, then that human protein may be used (especially in humans) for

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purposes analogous to the proposed use of the mouse protein in mice. Moreover, a specific binding fragment of an appropriate strand of the corresponding human gene (gDNA or cDNA) could be labeled and used as a hybridization probe (especially against samples of human mRNA or cDNA).

In determining whether the disclosed genes (gDNA or cDNA) have significant similarities to known DNAs (and their translated AA sequences to known proteins), one would generally use the disclosed gene as a query sequence in a search of a sequence database. The results of several such searches are set forth in the Examples. Such results are dependent, to some degree, on the search parameters. Preferred parameters are set forth in Example 1. The results are also dependent on the content of the database. While the raw similarity score of a particular target (database) sequence will not vary with content (as long as it remains in the database), its informational value (in bits), expected value, and relative ranking can change. Generally speaking, the changes are small.

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It will be appreciated that the nucleic acid and protein databases keep growing. Hence a later search may identify high scoring target sequences which were not uncovered by an earlier search because the target sequences were not previously part of a database.

Hence, in a preferred embodiment, the cognate DNAs and proteins include not only those set forth in the examples, but those which would have been highly ranked (top ten, more preferably top three, even more preferably top two, most preferably the top one) in a search run with the same parameters on the date of filing of this application.

If the known mouse or human database DNA appears to be a partial sequence (that is, partial relative to a cDNA or gDNA encoding the whole naturally occurring protein), it may be used as a hybridization probe to isolate the full-length DNA. If the partial DNA encodes a biologically functional fragment of the cognate protein, it may be used in a manner

similar to the full length DNA, i.e., to produce the functional fragment.

If we have indicated that an antagonist of a protein or other molecule is useful, then such an antagonist may be obtained by preparing a combinatorial library, as described below, of potential antagonists, and screening the library members for binding to the protein or other molecule in question. The binding members may then be further screened for the ability to antagonize the biological activity of the target. The antagonists may be used therapeutically, or, in suitably labeled or immobilized form, diagnostically.

If the identified mouse or human database DNA is related to a known protein, then substances known to interact with that protein (e.g., agonists, antagonists, substrates, receptors, second messengers, regulators, and so forth), and binding molecules which bind them, are also of utility. Such binding molecules can likewise be identified by screening a combinatorial library.

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Isolation of Full Length DNAs Using Partial DNAs as probes

If it is determined that a DNA of the present invention is a partial DNA, and the cognate full length DNA is not listed in a sequence database, the available DNA may be used as a hybridization probe to isolate the full-length DNA from a suitable DNA library.

Stringent hybridization conditions are appropriate, that is, conditions in which the hybridization temperature is 5-10 deg. C. below the Tm of the DNA as a perfect duplex.

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Identification and Isolation of Homologous Genes Using a DNA Probe

It may be that the sequence databases available do not include the sequence of any homologous gene (cDNA or gDNA), or at least of the homologous gene for a species of interest. However, given the cDNAs set forth above, one may readily obtain the homologous gene.

The possession of one DNA (the "starting DNA") greatly facilitates the isolation of homologous DNAs. If only a

partial DNA is known, this partial DNA may first be used as a probe to isolate the corresponding full length DNA for the same species, and that the latter may be used as the starting DNA in the search for homologous genes.

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The starting DNA, or a fragment thereof, is used as a hybridization probe to screen a cDNA or genomic DNA library for clones containing inserts which encode either the entire homologous protein, or a recognizable fragment thereof. The minimum length of the hybridization probe is dictated by the need for specificity. If the size of the library in bases is L, and the GC content is 50%, then the probe should have a length of at least 1, where $L=4^1$. This will yield, on average, a single perfect match in random DNA of L bases. The human cDNA library is about 10^8 bases and the human genomic DNA library is about 10^{10} bases.

The library is preferably derived from an organism which is known, on biochemical evidence, to produce a homologous protein, and more preferably from the genomic DNA or mRNA of cells of that organism which are likely to be relatively high producers of that protein. A cDNA library (which is derived from an mRNA library) is especially preferred.

If the organism in question is known to have substantially different codon preferences from that of the organism whose relevant cDNA or genomic DNA is known, a synthetic hybridization probe may be used which encodes the same amino acid sequence but whose codon utilization is more similar to that of the DNA of the target organism. Alternatively, the synthetic probe may employ inosine as a substitute for those bases which are most likely to be divergent, or the probe may be a mixed probe which mixes the codons for the source DNA with the preferred codons (encoding the same amino acid) for the target organism.

By routine methods, the Tm of a perfect duplex of starting DNA is determined. One may then select a hybridization temperature which is sufficiently lower than the perfect duplex Tm to allow hybridization of the starting DNA (or other probe) to a target DNA which is divergent from the starting DNA. A 1% sequence divergence typically lowers

42

the Tm of a duplex by 1-2°C, and the DNAs encoding homologous proteins of different species typically have sequence identities of around 50-80%. Preferably, the library is screened under conditions where the temperature is at least 20°C., more preferably at least 50°C., below the perfect duplex Tm. Since salt reduces the Tm, one ordinarily would carry out the search for DNAs encoding highly homologous proteins under relatively low salt hybridization conditions, e.g., <1M NaCl. The higher the salt concentration, and/or the lower the temperature, the greater the sequence divergence which is tolerated.

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For the use of probes to identify homologous genes in other species, see, e.g., Schwinn, et al., J. Biol. Chem., 265:8183-89 (1990) (hamster 67-bp cDNA probe vs. human leukocyte genomic library; human 0.32kb DNA probe vs. bovine brain cDNA library, both with hybridization at 42°C in 6xSSC); Jenkins et al., J. Biol. Chem., 265:19624-31 (1990) (Chicken 770-bp cDNA probe vs. human genomic libraries; hybridization at 40°C in 50% formamide and 5xSSC); Murata et al., J. Exp. Med., 175:341-51 (1992) (1.2-kb mouse cDNA probe v. human eosinophil cDNA library; hybridization at 65°C in 6xSSC); Guyer et al., J. Biol. Chem., 265:17307-17 (1990) (2.95-kb human genomic DNA probe vs. porcine genomic DNA library; hybridization at 42°C in 5xSSC). The conditions set forth in these articles may each be considered suitable for the purpose of isolating homologous genes.

Corresponding (Homologous) Proteins and DNAs:

In the case of a gene chip, the manufacturer of the gene chip determines which DNA to place at each position on the chip. This DNA may correspond in sequence to a genomic DNA, a cDNA, or a fragment of genomic or cDNA, and may be natural, synthetic or partially natural and partially synthetic in origin. The manufacturer of the gene chip will normally identify the DNA for a mouse gene chip as corresponding to a particular mouse gene, in which case it will be assumed that the alignments of chip DNA to mouse gene satisfies the homology criteria of the invention.

WO 2005/082398

Usually, the gene chip manufacturer will provide a sequence database accession number for the mouse DNA. If so, to identify the corresponding mouse protein, we will first inspect the database record for that mouse DNA. Often, the mouse protein accession number will appear in that record or in a linked record. If it doesn't, the corresponding mouse protein can be identified by performing a BlastX search on a mouse protein database with the mouse database DNA sequence as the query sequence. Even if the protein sequence is not in the database, if the DNA sequence comprises a full-length coding sequence, the corresponding protein can be identified by translating the coding sequence in accordance with the Genetic Code.

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A human protein can be said to be identifiable as corresponding (homologous) to a gene chip DNA if it is identified as corresponding (homologous) to the mouse gene (gDNA or cDNA, whole or partial) identified by the gene chip manufacturer as corresponding to that gene chip DNA.

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In turn, it is identifiable as corresponding (homologous) to said identified mouse gene, if

- (1) it can be aligned by BlastX directly to that mouse gene, and/or
- (2) it is encoded by a human gene, or can be aligned to a human gene by BlastX, which in turn can be aligned by BlastN to said mouse gene and/or

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(3) it can be aligned by BlastP to a mouse protein, the latter being encoded by said mouse gene, or aligned to said mouse gene BlastX,

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where any alignment by BlastN, BlastP or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone)

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is less than e-10. (Note that because this is a negative exponent, a value such as e-50 is less than e-10.)

WO 2005/082398

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Desirably, two or all three of these conditions (1)-(3) are satisfied for the corresponding (homologous) human genes and proteins.

A human gene is corresponding (homologous) to a mouse gene chip DNA, and hence to said identified mouse gene (or cDNA) and protein, if it encodes a corresponding (homologous) human protein as defined above, or it can be aligned by BlastN to said mouse gene.

Preferably, for at least one of conditions (1)-(3), the E value is less than e-50, more preferably less than e-60, still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100. Desirably, it is true for two or even all three of these conditions.

In constructing Master table 1, we generally used a BlastX (mouse gene vs. human protein) alignment E value cutoff of e-50. However, if there were no human proteins with that good an alignment to the mouse DNA in question, or if there were other reasons for including a particular human protein (e.g., a known functionality supportive of the observed differential cognate mouse protein expression), then a human protein with a score worse (i.e., higher) than e-50 may appear in Master Table 1.

If the manufacturer of the gene chip identifies the gene chip DNA as corresponding to an EST, or other DNA which is not a full-length mouse gene or cDNA, a longer (possibly full length) mouse gene or cDNA may be identified by a BlastN search of the mouse DNA database. Alternatively, the identified DNA may be used to conduct a BlastN search of a human DNA database, or a BlastX search of a mouse or human protein database.

Thus, more generally, a human protein can be said to be identifiable as corresponding (homologous) to a gene chip

DNA, or to a DNA identified by the manufacturer as corresponding to that gene chip DNA, if

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- (1') it can be aligned directly to the gene chip or corresponding manufacturer identified DNA by BlastX. and/or
- (2') it can be aligned to a human gene/cDNA by BlastX, whose genomic DNA (gDNA) or cDNA (DNA complementary to messenger RNA) in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or
- (3') it can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN, and/or
- (4') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to the gene chip or corresponding manufacturer identified DNA by BlastX, and/or
- (5') it can be aligned to a mouse protein by BlastP, which in turn can be aligned to a mouse gene/cDNA by BlastX, whose gDNA or cDNA can in turn be aligned to the gene chip or corresponding manufacturer identified DNA by BlastN;
- where any alignment by BlastN, BlastP, or BlastX is in accordance with the default parameters set forth below, and the expected value (E) of each alignment (the probability that such an alignment would have occurred by chance alone) is less than e-10. (Note that because this is a negative exponent, a value such as e-50 is less than e-10.)

Preferably, two, three, four or all five of conditions (1')-(5') are satisfied.

Preferably, for at least one of conditions (1')-(5'), for at least the final alignment (i.e., vs. the human protein), the E value is less than e-50, more preferably less than e-60, still more preferably less than e-70, even more preferably less than e-80, considerably more preferably less than e-90, and most preferably less than e-100.

Desirably, one or more of these standards of preference are met for two, three, four or all five of conditions (1')-(5'). In particular, for those conditions in which the gene chip or corresponding manufacturer identified DNA is indirectly connected to the human protein by virtue of two or more successive alignments, the E value is preferably, so limited for all of said alignments in the connecting chain.

A human gene corresponds (is homologous) to a gene chip DNA or manufacturer identified corresponding DNA if it encodes a homologous human protein as defined above, or if it can be aligned either directly to that DNA, or indirectly through a mouse gene which can be aligned to said DNA, according to the conditions set forth above.

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Master table 1 assembles a list of human protein corresponding to each of the mouse DNAs/proteins identified as related to the chip DNA. These human proteins form a set and can be given a percentile rank, with respect to E value, within that set. The human proteins of the present invention preferably are those scorers with a percentile rank of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

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For each mouse gene (gDNA or cDNA) in Master Table 1, there is a particular human protein which provides the best alignment match as measured by BlastX, i.e., the human protein with the best score (lowest e-value). These human proteins form a subset of the set above and can be given a percentile rank within that subset, e.g., the human proteins with scores in the top 10% of that subset have a percentile rank of 90% or higher.

The human proteins of the present invention preferably are those best scorer subset proteins with a percentile rank within the subset of at least 50%, more preferably at least 60%, still more preferably at least 70%, even more preferably at least 80%, and most preferably at least 90%.

BlastN and BlastX report very low expected values as "0.0". This does not truly mean that the expected value is exactly zero (since any alignment could occur by chance), but merely that it is so infinitesimal that it is not reported. The documentation does not state the cutoff value, but alignments with explicit E values as low as e-178 (624 bits) have been reported as nonzero values, while a score of 636 bits was reported as "0.0".

Functionally homologous human proteins are also of interest. A human protein may be said to be functionally homologous to the mouse gene if the human protein has at least one biological activity in common with the mouse protein encoded by said mouse gene.

The human proteins of interest also include those that are substantially and/or conservatively identical (as defined below) to the homologous and/or functionally homologous human proteins defined above.

Degree of Differential Expression

The degree of differential expression may be expressed as the ratio of the higher expression level to the lower expression level. Preferably, this is at least 2-fold, and more preferably, it is higher, such as at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold.

Most preferably, the human protein of interest corresponds to a mouse gene for which the degree of differential expression places it among the top 10% of the mouse genes in the appropriate subtable.

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WO 2005/082398

If a gene is down-regulated in more favored mammals, or up-regulated in less favored mammals, (i.e., an "unfavorable gene") then several utilities are apparent.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Elevated levels are indicative of progression, or propensity to progression, to a less favored state, and clinicians may take appropriate preventative, curative or ameliorative action.

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Secondly, the messenger RNA product (or equivalent cDNA), the protein product, or a binding molecule specific for that product (e.g., an antibody which binds the product), or a downstream product which mediates the activity (e.g., a signaling intermediate) or a binding molecule (e.g., an antibody) therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said nucleic acid product, protein product, or downstream product (e.g., a signaling intermediate). Again, elevated levels are indicative of a present or future problem.

Thirdly, an agent which down-regulates expression of the gene may be used to reduce levels of the corresponding protein and thereby inhibit further damage. This agent could inhibit transcription of the gene in the subject, or translation of the corresponding messenger RNA. inhibitors of transcription and translation include antisense molecules and repressor molecules. could also inhibit a post-translational modification (e.g., glycosylation, phosphorylation, cleavage, GPI attachment) required for activity, or post-translationally modify the protein so as to inactivate it. Or it could be an agent which down- or up-regulated a positive or negative regulatory gene, respectively.

Fourthly, an agent which is an antagonist of the messenger RNA product or protein product of the gene, or of a downstream product through which its activity is

manifested (e.g., a signaling intermediate), may be used to inhibit its activity.

This antagonist could be an antibody, a peptide, a peptide, a nucleic acid, a peptide nucleic acid (PNA) oligomer, a small organic molecule of a kind for which a combinatorial library exists (e.g., a benzodiazepine), etc. An antagonist is simply a binding molecule which, by binding, reduces or abolishes the undesired activity of its target. The antagonist, if not an oligomeric molecule, is preferably less than 1000 daltons, more preferably less than 500 daltons.

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Fifthly, an agent which degrades, or abets the degradation of, that messenger RNA, its protein product or a downstream product which mediates its activity (e.g., a signaling intermediate), may be used to curb the effective period of activity of the protein.

If a gene is <u>up</u>-regulated in more favored mammals, or <u>down</u>-regulated in less favored animals then the utilities are converse to those stated above.

First, the complementary strand of the gene, or a portion thereof, may be used in labeled form as a hybridization probe to detect messenger RNA and thereby monitor the level of expression of the gene in a subject. Depressed levels are indicative of damage, or possibly of a propensity to damage, and clinicians may take appropriate preventative, curative or ameliorative action.

Secondly, the messenger RNA product, the equivalent cDNA, protein product, or a binding molecule specific for those products, or a downstream product, or a signaling intermediate, or a binding molecule therefor, may be used, preferably in labeled or immobilized form, as an assay reagent in an assay for said protein product or downstream product. Again, depressed levels are indicative of a present or future problem.

Thirdly, an agent which up-regulates expression of the gene may be used to increase levels of the corresponding protein and thereby inhibit further progression to a less favored state. By way of example, it could be a vector which carries a copy of the gene, but which expresses the

gene at higher levels than does the endogenous expression system. Or it could be an agent which up- or down-regulates a positive or negative regulatory gene.

Fourthly, an agent which is an agonist of the protein product of the gene, or of a downstream product through which its activity (of inhibition of progression to a less favored state) is manifested, or of a signaling intermediate may be used to foster its activity.

Fifthly, an agent which inhibits the degradation of that protein product or of a downstream product or of a signaling intermediate may be used to increase the effective period of activity of the protein.

Mutant Proteins

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The present invention also contemplates mutant proteins (peptides) which are substantially identical (as defined below) to the parental protein (peptide). In general, the fewer the mutations, the more likely the mutant protein is to retain the activity of the parental protein. The effect of mutations is usually (but not always) additive. Certain individual mutations are more likely to be tolerated than others.

A protein is more likely to tolerate a mutation which

- (a) is a substitution rather than an insertion or deletion;
- (b) is an insertion or deletion at the terminus, rather than internally, or, if internal, is at a domain boundary, or a loop or turn, rather than in an alpha helix or beta strand;
- (c) affects a surface residue rather than an interior residue;
- (d) affects a part of the molecule distal to the binding site;
- (e) is a substitution of one amino acid for another of similar size, charge, and/or hydrophobicity, and does not destroy a disulfide bond or other crosslink; and

(f) is at a site which is subject to substantial variation among a family of homologous proteins to which the protein of interest belongs.

These considerations can be used to design functional mutants.

Surface vs. Interior Residues

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Charged amino acid residues almost always lie on the surface of the protein. For uncharged residues, there is less certainty, but in general, hydrophilic residues are partitioned to the surface and hydrophobic residues to the interior. Of course, for a membrane protein, the membranespanning segments are likely to be rich in hydrophobic residues.

Surface residues may be identified experimentally by various labeling techniques, or by 3-D structure mapping techniques like X-ray diffraction and NMR. A 3-D model of a homologous protein can be helpful.

Binding Site Residues 20

Residues forming the binding site may be identified by (1) comparing the effects of labeling the surface residues before and after complexing the protein to its target, (2) labeling the binding site directly with affinity ligands, (3) fragmenting the protein and testing the fragments for binding activity, and (4) systematic mutagenesis (e.g., alanine-scanning mutagenesis) to determine which mutants destroy binding. If the binding site of a homologous protein is known, the binding site may be postulated by analogy.

Protein libraries may be constructed and screened that a large family (e.g., 108) of related mutants may be evaluated simultaneously.

Hence, the mutations are preferably conservative modifications as defined below.

"Substantially Identical"

A mutant protein (peptide) is substantially identical to a reference protein (peptide) if (a) it has at least 10%

of a specific binding activity or a non-nutritional biological activity of the reference protein, and (b) is at least 50% identical in amino acid sequence to the reference protein (peptide). It is "substantially structurally identical" if condition (b) applies, regardless of (a).

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Percentage amino acid identity is determined by aligning the mutant and reference sequences according to a rigorous dynamic programming algorithm which globally aligns their sequences to maximize their similarity, the similarity being scored as the sum of scores for each aligned pair according to an unbiased PAM250 matrix, and a penalty for each internal gap of -12 for the first null of the gap and -4 for each additional null of the same gap. The percentage identity is the number of matches expressed as a percentage of the adjusted (i.e., counting inserted nulls) length of the reference sequence.

A mutant DNA sequence is substantially identical to a reference DNA sequence if they are structural sequences, and encoding mutant and reference proteins which are substantially identical as described above.

If instead they are regulatory sequences, they are substantially identical if the mutant sequence has at least 10% of the regulatory activity of the reference sequence, and is at least 50% identical in nucleotide sequence to the reference sequence. Percentage identity is determined as for proteins except that matches are scored +5, mismatches -4, the gap open penalty is -12, and the gap extension penalty (per additional null) is -4.

More preferably, the sequence is not merely substantially identical but rather is at least 51%, at least 66%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical in sequence to the reference sequence.

DNA sequences may also be considered "substantially identical" if they hybridize to each other under stringent conditions, i.e., conditions at which the Tm of the heteroduplex of the one strand of the mutant DNA and the more complementary strand of the reference DNA is not in

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excess of 10°C. less than the Tm of the reference DNA homoduplex. Typically this will correspond to a percentage identity of 85-90%.

5 "Conservative Modifications"

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"Conservative modifications" are defined as

- (a) conservative substitutions of amino acids as hereafter defined; or
- (b) single or multiple insertions (extension) or deletions (truncation) of amino acids at the termini.

Conservative modifications are preferred to other modifications. Conservative substitutions are preferred to other conservative modifications.

"Semi-Conservative Modifications" are modifications which are not conservative, but which are (a) semi-conservative substitutions as hereafter defined; or (b) single or multiple insertions or deletions internally, but at interdomain boundaries, in loops or in other segments of relatively high mobility. Semi-conservative modifications are preferred to nonconservative modifications. Semi-conservative substitutions are preferred to other semi-conservative modifications.

Non-conservative substitutions are preferred to other non-conservative modifications.

The term "conservative" is used here in an <u>a priori</u> sense, i.e., modifications which would be <u>expected</u> to preserve 3D structure and activity, based on analysis of the naturally occurring families of homologous proteins and of past experience with the effects of deliberate mutagenesis, rather than <u>post facto</u>, a modification already known to conserve activity. Of course, a modification which is conservative <u>a priori</u> may, and usually is, also conservative <u>post facto</u>.

Preferably, except at the termini, no more than about five amino acids are inserted or deleted at a particular locus, and the modifications are outside regions known to contain binding sites important to activity.

PCT/US2005/005596 WO 2005/082398

Preferably, insertions or deletions are limited to the termini.

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A conservative substitution is a substitution of one amino acid for another of the same exchange group, the exchange groups being defined as follows

- I Gly, Pro, Ser, Ala (Cys) (and any nonbiogenic, neutral amino acid with a hydrophobicity not exceeding that of the aforementioned a.a.'s)
- Arg, Lys, His (and any nonbiogenic, positively-II charged amino acids)
- Asp, Glu, Asn, Gln (and any nonbiogenic negatively-charged amino acids)
- Leu, Ile, Met, Val (Cys) (and any nonbiogenic, IV aliphatic, neutral amino acid with a hydrophobicity too high for I above)
- Phe, Trp, Tyr (and any nonbiogenic, aromatic V neutral amino acid with a hydrophobicity too high for I above).

Note that Cys belongs to both I and IV.

Residues Pro, Gly and Cys have special conformational Cys participates in formation of disulfide bonds. Gly imparts flexibility to the chain. Pro imparts rigidity to the chain and disrupts α helices. These residues may be essential in certain regions of the polypeptide, but substitutable elsewhere.

One, two or three conservative substitutions are more likely to be tolerated than a larger number.

"Semi-conservative substitutions" are defined herein as being substitutions within supergroup I/II/III or within supergroup IV/V, but not within a single one of groups I-V. They also include replacement of any other amino acid with alanine. If a substitution is not conservative, it preferably is semi-conservative.

"Non-conservative substitutions" are substitutions which are not "conservative" or "semi-conservative".

"Highly conservative substitutions" are a subset of conservative substitutions, and are exchanges of amino acids within the groups Phe/Tyr/Trp, Met/Leu/Ile/Val, His/Arg/Lys, Asp/Glu and Ser/Thr/Ala. They are more likely to be

tolerated than other conservative substitutions. Again, the smaller the number of substitutions, the more likely they are to be tolerated.

"Conservatively Identical"

A protein (peptide) is conservatively identical to a reference protein (peptide) it differs from the latter, if at all, solely by conservative modifications, the protein (peptide remaining at least seven amino acids long if the reference protein (peptide) was at least seven amino acids long.

A protein is at least semi-conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by semi-conservative or conservative modifications.

A protein (peptide) is nearly conservatively identical to a reference protein (peptide) if it differs from the latter, if at all, solely by one or more conservative modifications and/or a single nonconservative substitution.

It is highly conservatively identical if it differs, if at all, solely by highly conservative substitutions. Highly conservatively identical proteins are preferred to those merely conservatively identical. An absolutely identical protein is even more preferred.

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The core sequence of a reference protein (peptide) is the largest single fragment which retains at least 10% of a particular specific binding activity, if one is specified, or otherwise of at least one specific binding activity of the referent. If the referent has more than one specific binding activity, it may have more than one core sequence, and these may overlap or not.

If it is taught that a peptide of the present invention may have a particular similarity relationship (e.g., markedly identical) to a reference protein (peptide), preferred peptides are those which comprise a sequence having that relationship to a core sequence of the reference protein (peptide), but with internal insertions or deletions

in either sequence excluded. Even more preferred peptides are those whose entire sequence has that relationship, with the same exclusion, to a core sequence of that reference protein (peptide).

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Library

The term "library" generally refers to a collection of chemical or biological entities which are related in origin, structure, and/or function, and which can be screened simultaneously for a property of interest.

Libraries may be classified by how they are constructed (natural vs. artificial diversity; combinatorial vs. noncombinatorial), how they are screened (hybridization, expression, display), or by the nature of the screened library members (peptides, nucleic acids, etc.).

In a "natural diversity" library, essentially all of the diversity arose without human intervention. This would be true, for example, of messenger RNA extracted from a nonengineered cell.

In a "synthetic diversity" library, essentially all of the diversity arose deliberately as a result of human intervention. This would be true for example of a combinatorial library; note that a small level of natural diversity could still arise as a result of spontaneous mutation. It would also be true of a noncombinatorial library of compounds collected from diverse sources, even if they were all natural products.

In a "non-natural diversity" library, at least some of the diversity arose deliberately through human intervention.

In a "controlled origin" library, the source of the diversity is limited in some way. A limitation might be to cells of a particular individual, to a particular species, or to a particular genus, or, more complexly, to individuals of a particular species who are of a particular age, sex, physical condition, geographical location, occupation and/or familial relationship. Alternatively or additionally, it might be to cells of a particular tissue or organ. Or it could be cells exposed to particular pharmacological,

57

environmental, or pathogenic conditions. Or the library could be of chemicals, or a particular class of chemicals, produced by such cells.

In a "controlled structure" library, the library members are deliberately limited by the production conditions to particular chemical structures. For example, if they are oligomers, they may be limited in length and monomer composition, e.g. hexapeptides composed of the twenty genetically encoded amino acids.

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Hybridization Library

In a hybridization library, the library members are nucleic acids, and are screened using a nucleic acid hybridization probe. Bound nucleic acids may then be amplified, cloned, and/or sequenced.

Expression Library

In an expression library, the screened library members are gene expression products, but one may also speak of an underlying library of genes encoding those products. The library is made by subcloning DNA encoding the library members (or portions thereof) into expression vectors (or into cloning vectors which subsequently are used to construct expression vectors), each vector comprising an expressible gene encoding a particular library member, introducing the expression vectors into suitable cells, and expressing the genes so the expression products are produced.

In one embodiment, the expression products are secreted, so the library can be screened using an affinity reagent, such as an antibody or receptor. The bound expression products may be sequenced directly, or their sequences inferred by, e.g., sequencing at least the variable portion of the encoding DNA.

In a second embodiment, the cells are lysed, thereby exposing the expression products, and the latter are screened with the affinity reagent.

In a third embodiment, the cells express the library members in such a manner that they are displayed on the

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surface of the cells, or on the surface of viral particles produced by the cells. (See display libraries, below).

In a fourth embodiment, the screening is not for the ability of the expression product to bind to an affinity reagent, but rather for its ability to alter the phenotype of the host cell in a particular detectable manner. Here, the screened library members are transformed cells, but there is a first underlying library of expression products which mediate the behavior of the cells, and a second underlying library of genes which encode those products.

Display Library

In a display library, the library members are each conjugated to, and displayed upon, a support of some kind. The support may be living (a cell or virus), or nonliving (e.g., a bead or plate).

If the support is a cell or virus, display will normally be effectuated by expressing a fusion protein which comprises the library member, a carrier moiety allowing integration of the fusion protein into the surface of the cell or virus, and optionally a lining moiety. In a variation on this theme, the cell coexpresses a first fusion comprising the library member and a linking moiety L1, and a second fusion comprising a linking moiety L2 and the carrier moiety. L1 and L2 interact to associate the first fusion with the second fusion and hence, indirectly, the library member with the surface of the cell or virus.

Soluble Library

In a soluble library, the library members are free in solution. A soluble library may be produced directly, or one may first make a display library and then release the library members from their supports.

Encapsulated Library

In an encapsulated library, the library members are inside cells or liposomes. Generally speaking, encapsulated libraries are used to store the library members for future use; the members are extracted in some way for screening

WO 2005/082398

purposes. However, if they differentially affect the phenotype of the cells, they may be screened indirectly by screening the cells.

5 <u>cDNA Library</u>

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A cDNA library is usually prepared by extracting RNA from cells of particular origin, fractionating the RNA to isolate the messenger RNA (mRNA has a poly(A) tail, so this is usually done by oligo-dT affinity chromatography), synthesizing complementary DNA (cDNA) using reverse transcriptase, DNA polymerase, and other enzymes, subcloning the cDNA into vectors, and introducing the vectors into cells. Often, only mRNAs or cDNAs of particular sizes will be used, to make it more likely that the cDNA encodes a functional polypeptide.

A cDNA library explores the natural diversity of the transcribed DNAs of cells from a particular source. It is not a combinatorial library.

A cDNA library may be used to make a hybridization library, or it may be used as an (or to make) expression library.

Genomic DNA Library

A genomic DNA library is made by extracting DNA from a particular source, fragmenting the DNA, isolating fragments of a particular size range, subcloning the DNA fragments into vectors, and introducing the vectors into cells.

Like a cDNA library, a genomic DNA library is a natural diversity library, and not a combinatorial library. A genomic DNA library may be used the same way as a cDNA library.

Synthetic DNA library

A synthetic DNA library may be screened directly (as a hybridization library), or used in the creation of an expression or display library of peptides/proteins.

Combinatorial Libraries

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The term "combinatorial library" refers to a library in which the individual members are either systematic or random combinations of a limited set of basic elements, the properties of each member being dependent on the choice and location of the elements incorporated into it. the members of the library are at least capable of being screened simultaneously. Randomization may be complete or partial; some positions may be randomized and others predetermined, and at random positions, the choices may be limited in a predetermined manner. The members of a combinatorial library may be oligomers or polymers of some kind, in which the variation occurs through the choice of monomeric building block at one or more positions of the oligomer or polymer, and possibly in terms of the connecting linkage, or the length of the oligomer or polymer, too. Or the members may be nonoligomeric molecules with a standard core structure, like the 1,4-benzodiazepine structure, with the variation being introduced by the choice of substituents at particular variable sites on the core structure. Or the members may be nonoligomeric molecules assembled like a jigsaw puzzle, but wherein each piece has both one or more variable moieties (contributing to library diversity) and one or more constant moieties (providing the functionalities for coupling the piece in question to other pieces).

Thus, in a typical combinatorial library, chemical building blocks are at least partially randomly combined into a large number (as high as 10¹⁵) of different compounds, which are then simultaneously screened for binding (or other) activity against one or more targets.

In a "simple combinatorial library", all of the members belong to the same class of compounds (e.g., peptides) and can be synthesized simultaneously. A "composite combinatorial library" is a mixture of two or more simple libraries, e.g., DNAs and peptides, or peptides, peptoids, and PNAs, or benzodiazepines and carbamates. The number of component simple libraries in a composite library will, of course, normally be smaller than the average number of members in each simple library, as otherwise the advantage of a library over individual synthesis is small.

Libraries of thousands, even millions, of random oligopeptides have been prepared by chemical synthesis (Houghten et al., Nature, 354:84-6(1991)), or gene expression (Marks et al., J Mol Biol, 222:581-97(1991)), displayed on chromatographic supports (Lam et al., Nature, 354:82-4(1991)), inside bacterial cells (Colas et al., Nature, 380:548-550 (1996)), on bacterial pili (Lu, Bio/Technology, 13:366-372(1990)), or phage (Smith, Science, .228:1315-7(1985)), and screened for binding to a variety of targets including antibodies (Valadon et al., J Mol Biol, 261:11-22(1996)), cellular proteins (Schmitz et al., J Mol Biol, 260:664-677(1996)), viral proteins (Hong and Boulanger, Embo J, 14:4714-4727(1995)), bacterial proteins (Jacobsson and Frykberg, Biotechniques, 18:878-885(1995)), nucleic acids (Cheng et al., Gene, 171:1-8(1996)), and plastic (Siani et al., J Chem Inf Comput Sci, 34:588-593 (1994)).

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Libraries of proteins (Ladner, USP 4,664,989), peptoids (Simon et al., Proc Natl Acad Sci U S A, 89:9367-71(1992)), nucleic acids (Ellington and Szostak, Nature, 246:818(1990)), carbohydrates, and small organic molecules (Eichler et al., Med Res Rev, 15:481-96(1995)) have also been prepared or suggested for drug screening purposes.

The first combinatorial libraries were composed of peptides or proteins, in which all or selected amino acid positions were randomized. Peptides and proteins can exhibit high and specific binding activity, and can act as catalysts. In consequence, they are of great importance in biological systems.

Nucleic acids have also been used in combinatorial libraries. Their great advantage is the ease with which a nucleic acid with appropriate binding activity can be amplified. As a result, combinatorial libraries composed of nucleic acids can be of low redundancy and hence, of high diversity.

There has also been much interest in combinatorial libraries based on small molecules, which are more suited to pharmaceutical use, especially those which, like benzodiazepines, belong to a chemical class which has

already yielded useful pharmacological agents. The techniques of combinatorial chemistry have been recognized as the most efficient means for finding small molecules that act on these targets. At present, small molecule combinatorial chemistry involves the synthesis of either pooled or discrete molecules that present varying arrays of functionality on a common scaffold. These compounds are grouped in libraries that are then screened against the target of interest either for binding or for inhibition of biological activity.

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The size of a library is the number of molecules in it. The simple diversity of a Library is the number of unique structures in it. There is no formal minimum or maximum diversity. If the library has a very low diversity, the library has little advantage over just synthesizing and screening the members individually. If the library is of very high diversity, it may be inconvenient to handle, at least without automatizing the process. The simple diversity of a library is preferably at least 10, 10E2, 10E3, 10E4, 10E6, 10E7, 10E8 or 10E9, the higher the better under most circumstances. The simple diversity is usually not more than 10E15, and more usually not more than 10E10.

The average sampling level is the size divided by the simple diversity. The expected average sampling level must be high enough to provide a reasonable assurance that, if a given structure were expected, as a consequence of the Library design, to be present, that the actual average sampling level will be high enough so that the structure, if satisfying the screening criteria, will yield a positive result when the library is screened. Thus, the preferred average sampling level is a function of the detection limit, which in turn is a function of the strength of the signal to be screened.

There are more complex measures of diversity than simple diversity. These attempt to take into account the degree of structural difference between the various unique sequences. These more complex measures are usually used in the context of small organic compound libraries, see below.

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The library members may be presented as solutes in solution, or immobilized on some form of support. In the latter case, the support may be living (cell, virus) or nonliving (bead, plate, etc.). The supports may be separable (cells, virus particles, beads) so that binding and nonbinding members can be separated, or nonseparable (plate). In the latter case, the members will normally be placed on addressable positions on the support. The advantage of a soluble library is that there is no carrier moiety that could interfere with the binding of the members to the support. The advantage of an immobilized library is that it is easier to identify the structure of the members which were positive.

When screening a soluble library, or one with a separable support, the target is usually immobilized. When screening a library on a nonseparable support, the target will usually be labeled.

Oligonucleotide Libraries

An oligonucleotide library is a combinatorial library, at least some of whose members are single-stranded oligonucleotides having three or more nucleotides connected by phosphodiester or analogous bonds. The oligonucleotides may be linear, cyclic or branched, and may include non-nucleic acid moieties. The nucleotides are not limited to the nucleotides normally found in DNA or RNA. For examples of nucleotides modified to increase nuclease resistance and chemical stability of aptamers, see Chart 1 in Osborne and Ellington, Chem. Rev., 97: 349-70 (1997). For screening of RNA, see Ellington and Szostak, Nature, 346: 818-22 (1990).

There is no formal minimum or maximum size for these oligonucleotides. However, the number of conformations which an oligonucleotide can assume increases exponentially with its length in bases. Hence, a longer oligonucleotide is more likely to be able to fold to adapt itself to a protein surface. On the other hand, while very long molecules can be synthesized and screened, unless they provide a much superior affinity to that of shorter molecules, they are not likely to be found in the selected population, for the

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reasons explained by Osborne and Ellington (1997). Hence, the libraries of the present invention are preferably composed of oligonucleotides having a length of 3 to 100 bases, more preferably 15 to 35 bases. The oligonucleotides in a given library may be of the same or of different lengths.

Oligonucleotide libraries have the advantage that libraries of very high diversity (e.g., 10¹⁵) are feasible, and binding molecules are readily amplified in vitro by polymerase chain reaction (PCR). Moreover, nucleic acid molecules can have very high specificity and affinity to targets.

In a preferred embodiment, this invention prepares and screens oligonucleotide libraries by the SELEX method, as described in King and Famulok, Molec. Biol. Repts., 20: 97-107 (1994); L. Gold, C. Tuerk. Methods of producing nucleic acid ligands, US#5595877; Oliphant et al. Gene 44:177 (1986).

The term "aptamer" is conferred on those oligonucleotides which bind the target protein. Such aptamers may be used to characterize the target protein, both directly (through identification of the aptamer and the points of contact between the aptamer and the protein) and indirectly (by use of the aptamer as a ligand to modify the chemical reactivity of the protein).

In a classic oligonuclotide, each nucleotide (monomeric unit) is composed of a phosphate group, a sugar moiety, and either a purine or a pyrimidine base. In DNA, the sugar is deoxyribose and in RNA it is ribose. The nucleotides are linked by 5'-3' phosphodiester bonds.

The deoxyribose phosphate backbone of DNA can be modified to increase resistance to nuclease and to increase penetration of cell membranes. Derivatives such as mono- or dithiophosphates, methyl phosphonates, boranophosphates, formacetals, carbamates, siloxanes, and dimethylenethio-sulfoxideo-and-sulfono-linked species are known in the art.

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A peptide is composed of a plurality of amino acid residues joined together by peptidyl (-NHCO-) bonds. A biogenic peptide is a peptide in which the residues are all genetically encoded amino acid residues; it is not necessary that the biogenic peptide actually be produced by gene expression.

Amino acids are the basic building blocks with which peptides and proteins are constructed. Amino acids possess both an amino group (-NH2) and a carboxylic acid group (-Many amino acids, but not all, have the alpha amino acid structure NH2-CHR-COOH, where R is hydrogen, or any of a variety of functional groups.

Twenty amino acids are genetically encoded: Arginine, Asparagine, Aspartic Acid, Cysteine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, and Valine. Of these, all save Glycine are optically isomeric, however, only the Lform is found in humans. Nevertheless, the D-forms of these amino acids do have biological significance; D-Phe, for example, is a known analgesic.

Many other amino acids are also known, including: 2-Aminoadipic acid; 3-Aminoadipic acid; beta-Aminopropionic acid; 2-Aminobutyric acid; 4-Aminobutyric acid (Piperidinic acid);6-Aminocaproic acid; 2-Aminoheptanoic acid; 2-Aminoisobutyric acid, 3-Aminoisobutyric acid; 2-Aminopimelic acid; 2,4-Diaminobutyric acid; Desmosine; 2,2'-Diaminopimelic acid; 2, 3-Diaminopropionic acid; N-Ethylglycine; N-Ethylasparagine; Hydroxylysine; allo-Hydroxylysine; 3-Hydroxyproline; 4-Hydroxyproline; Isodesmosine; allo-Isoleucine; N-Methylglycine (Sarcosine); N-Methylisoleucine; N-Methylvaline; Norvaline; Norleucine; and Ornithine.

Peptides are constructed by condensation of amino acids and/or smaller peptides. The amino group of one amino acid (or peptide) reacts with the carboxylic acid group of a second amino acid (or peptide) to form a peptide (-NHCO-) bond, releasing one molecule of water. Therefore, when an amino acid is incorporated into a peptide, it should,

technically speaking, be referred to as an amino acid residue. The core of that residue is the moiety which excludes the -NH and -CO linking functionalities which connect it to other residues. This moiety consists of one or more main chain atoms (see below) and the attached side chains.

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The main chain moiety of each amino acid consists of the -NH and -CO linking functionalities and a core main chain moiety. Usually the latter is a single carbon atom. However, the core main chain moiety may include additional carbon atoms, and may also include nitrogen, oxygen or sulfur atoms, which together form a single chain. In a preferred embodiment, the core main chain atoms consist solely of carbon atoms.

The side chains are attached to the core main chain atoms. For alpha amino acids, in which the side chain is attached to the alpha carbon, the C-1, C-2 and N-2 of each residue form the repeating unit of the main chain, and the word "side chain" refers to the C-3 and higher numbered carbon atoms and their substituents. It also includes H atoms attached to the main chain atoms.

Amino acids may be classified according to the number of carbon atoms which appear in the main chain between the carbonyl carbon and amino nitrogen atoms which participate in the peptide bonds. Among the 150 or so amino acids which occur in nature, alpha, beta, gamma and delta amino acids are known. These have 1-4 intermediary carbons. Only alpha amino acids occur in proteins. Proline is a special case of an alpha amino acid; its side chain also binds to the peptide bond nitrogen.

For beta and higher order amino acids, there is a choice as to which main chain core carbon a side chain other than H is attached to. The preferred attachment site is the C-2 (alpha) carbon, i.e., the one adjacent to the carboxyl carbon of the -CO linking functionality. It is also possible for more than one main chain atom to carry a side chain other than H. However, in a preferred embodiment, only one main chain core atom carries a side chain other than H.

A main chain carbon atom may carry either one or two side chains; one is more common. A side chain may be attached to a main chain carbon atom by a single or a double bond; the former is more common.

A simple combinatorial peptide library is one whose members are peptides having three or more amino acids connected via peptide bonds.

The peptides may be linear, branched, or cyclic, and may covalently or noncovalently include nonpeptidyl moieties. The amino acids are not limited to the naturally occurring or to the genetically encoded amino acids.

A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues.

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Cyclic Peptides

Many naturally occurring peptides are cyclic. Cyclization is a common mechanism for stabilization of peptide conformation thereby achieving improved association of the peptide with its ligand and hence improved biological activity. Cyclization is usually achieved by intra-chain cystine formation, by formation of peptide bond between side chains or between N- and C- terminals. Cyclization was usually achieved by peptides in solution, but several publications have appeared that describe cyclization of peptides on beads.

A peptide library may be an oligopeptide library or a protein library.

Ol**ig**opeptides

Preferably, the oligopeptides are at least five, six, seven or eight amino acids in length. Preferably, they are composed of less than 50, more preferably less than 20 amino acids.

In the case of an oligopeptide library, all or just some of the residues may be variable. The oligopeptide may be unconstrained, or constrained to a particular conformation by, e.g., the participation of constant

cysteine residues in the formation of a constraining disulfide bond.

Proteins

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Proteins, like oligopeptides, are composed of a plurality of amino acids, but the term protein is usually reserved for longer peptides, which are able to fold into a stable conformation. A protein may be composed of two or more polypeptide chains, held together by covalent or noncovalent crosslinks. These may occur in a homooligomeric or a heterooligomeric state.

A peptide is considered a protein if it (1) is at least 50 amino acids long, or (2) has at least two stabilizing covalent crosslinks (e.g., disulfide bonds). Thus, conotoxins are considered proteins.

Usually, the proteins of a protein library will be characterizable as having both constant residues (the same for all proteins in the library) and variable residues (which vary from member to member). This is simply because, for a given range of variation at each position, the sequence space (simple diversity) grows exponentially with the number of residue positions, so at some point it becomes inconvenient for all residues of a peptide to be variable positions. Since proteins are usually larger than oligopeptides, it is more common for protein libraries than oligopeptide libraries to feature variable positions.

In the case of a protein library, it is desirable to focus the mutations at those sites which are tolerant of mutation. These may be determined by alanine scanning mutagenesis or by comparison of the protein sequence to that of homologous proteins of similar activity. It is also more likely that mutation of surface residues will directly affect binding. Surface residues may be determined by inspecting a 3D structure of the protein, or by labeling the surface and then ascertaining which residues have received labels. They may also be inferred by identifying regions of high hydrophilicity within the protein.

WO 2005/082398

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Because proteins are often altered at some sites but not others, protein libraries can be considered a special case of the biased peptide library.

There are several reasons that one might screen a protein library instead of an oligopeptide library, including (1) a particular protein, mutated in the library, has the desired activity to some degree already, and (2) the oligopeptides are not expected to have a sufficiently high affinity or specificity since they do not have a stable conformation.

When the protein library is based on a parental protein which does not have the desired activity, the parental protein will usually be one which is of high stability (melting point >= 50 deg. C.) and/or possessed of hypervariable regions.

The variable domains of an antibody possess hypervariable regions and hence, in some embodiments, the protein library comprises members which comprise a mutant of VH or VL chain, or a mutant of an antigen-specific binding fragment of such a chain. VH and VL chains are usually each about 110 amino acid residues, and are held in proximity by a disulfide bond between the adjoing CL and CH1 regions to form a variable domain. Together, the VH, VL, CL and CH1 form an Fab fragment.

In human heavy chains, the hypervariable regions are at 31-35, 49-65, 98-111 and 84-88, but only the first three are involved in antigen binding. There is variation among VH and VL chains at residues outside the hypervariable regions, but to a much lesser degree.

A sequence is considered a mutant of a VH or VL chain if it is at least 80% identical to a naturally occurring VH or VL chain at all residues outside the hypervariable region.

In a preferred embodiment, such antibody library members comprise both at least one VH chain and at least one VL chain, at least one of which is a mutant chain, and which chains may be derived from the same or different antibodies. The VH and VL chains may be covalently joined by a suitable linker moiety, as in a "single chain antibody", or they may

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be noncovalently joined, as in a naturally occurring variable domain.

If the joining is noncovalent, and the library is displayed on cells or virus, then either the VH or the VL chain may be fused to the carrier surface/coat protein. The complementary chain may be co-expressed, or added exogenously to the library.

The members may further comprise some or all of an antibody constant heavy and/or constant light chain, or a mutant thereof.

Peptoid Library

A peptoid is an analogue of a peptide in which one or more of the peptide bonds (-NH-CO-) are replaced by pseudopeptide bonds, which may be the same or different. It is not necessary that all of the peptide bonds be replaced, i.e., a peptoid may include one or more conventional amino acid residues, e.g., proline.

A peptide bond has two small divalent linker elements, -NH- and -CO-. Thus, a preferred class of psuedopeptide bonds are those which consist of two small divalent linker elements. Each may be chosen independently from the group consisting of amine (-NH-), substituted amine (-NR-), carbonyl (-CO-), thiocarbonyl (-CS-), methylene (-CH2-), monosubstituted methylene (-CHR-), disubstituted methylene (-CR1R2-), ether (-O-) and thioether (-S-). The more preferred pseudopeptide bonds include:

N-modified -NRCOCarba Ψ -CH₂-CH₂Depsi Ψ -CO-OHydroxyethylene Ψ -CHOH-CH₂Ketomethylene Ψ -CO-CH₂Methylene-Oxy -CH₂-OReduced -CH₂-NHThiomethylene -CH₂-SThiopeptide -CS-NHRetro-Inverso -CO-NH-

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A single peptoid molecule may include more than one kind of pseudopeptide bond.

For the purposes of introducing diversity into a peptoid library, one may vary (1) the side chains attached to the core main chain atoms of the monomers linked by the pseudopeptide bonds, and/or (2) the side chains (e.g., the -R of an -NRCO-) of the pseudopeptide bonds. Thus, in one embodiment, the monomeric units which are not amino acid residues are of the structure -NR1-CR2-CO-, where at least one of R1 and R2 are not hydrogen. If there is variability in the pseudopeptide bond, this is most conveniently done by using an -NRCO- or other pseudopeptide bond with an R group, and varying the R group. In this event, the R group will usually be any of the side chains characterizing the amino acids of peptides, as previously discussed.

If the R group of the pseudopeptide bond is not variable, it will usually be small, e.g., not more than 10 atoms (e.g., hydroxyl, amino, carboxyl, methyl, ethyl, propyl).

If the conjugation chemistries are compatible, a simple combinatorial library may include both peptides and peptoids.

Peptide Nucleic Acid Library

A PNA oligomer is here defined as one comprising a plurality of units, at least one of which is a PNA monomer which comprises a side chain comprising a nucleobase. For nucleobases, see USP 6,077,835.

The classic PNA oligomer is composed of (2-aminoethyl)glycine units, with nucleobases attached by methylene carbonyl linkers. That is, it has the structure

$$H (-HN-CH2-CH2-N(-CO-CH2-B)-CH2-CO-)n -OH$$

where the outer parenthesized substructure is the PNA monomer.

In this structure, the nucleobase B is separated from the backbone N by three bonds, and the points of attachment

72

of the side chains are separated by six bonds. The nucleobase may be any of the bases included in the nucleotides discussed in connection with oligonucleotide libraries. The bases of nucleotides A, G, T, C and U are preferred.

A PNA oligomer may further comprise one or more amino acid residues, especially glycine and proline.

One can readily envision related molecules in which (1) the -COCH2- linker is replaced by another linker, especially one composed of two small divalent linkers as defined previously, (2) a side chain is attached to one of the three main chain carbons not participating in the peptide bond (either instead or in addition to the side chain attached to the N of the classic PNA); and/or (3) the peptide bonds are replaced by pseudopeptide bonds as disclosed previously in the context of peptoids.

PNA oligomer libraries have been made; see e.g. Cook, 6,204,326.

Small Organic Compound Library

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The small organic compound library ("compound library", for short) is a combinatorial library whose members are suitable for use as drugs if, indeed, they have the ability to mediate a biological activity of the target protein.

Peptides have certain disadvantages as drugs. These include susceptibility to degradation by serum proteases, and difficulty in penetrating cell membranes. Preferably, all or most of the compounds of the compound library avoid, or at least do not suffer to the same degree, one or more of the pharmaceutical disadvantages of peptides.

In designing a compound library, it is helpful to bear in mind the methods of molecular modification typically used to obtain new drugs. Three basic kinds of modification may be identified: disjunction, in which a lead drug is simplified to identify its component pharmacophoric, moieties; conjunction, in which two or more known pharmacophoric moieties, which may be the same or different, are associated, covalently or noncovalently, to form a new drug; and alteration, in which one moiety is replaced by

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another which may be similar or different, but which is not in effect a disjunction or conjunction. The use of the terms "disjunction", "conjunction" and "alteration" is intended only to connote the structural relationship of the end product to the original leads, and not how the new drugs are actually synthesized, although it is possible that the two are the same.

The process of disjunction is illustrated by the evolution of neostigmine (1931) and edrophonium (1952) from physostigmine (1925). Subsequent conjunction is illustrated by demecarium (1956) and ambenonium (1956).

Alterations may modify the size, polarity, or electron distribution of an original moiety. Alterations include ring closing or opening, formation of lower or higher homologues, introduction or saturation of double bonds, introduction of optically active centers, introduction, removal or replacement of bulky groups, isosteric or bioisosteric substitution, changes in the position or orientation of a group, introduction of alkylating groups, and introduction, removal or replacement of groups with a view toward inhibiting or promoting inductive (electrostatic) or conjugative (resonance) effects.

Thus, the substituents may include electron acceptors and/or electron donors. Typical electron donors (+I) include $-CH_3$, $-CH_2R$, $-CHR_2$, $-CR_3$ and $-COO^-$. Typical electron acceptors (-I) include $-NH_3+$, $-NR_3+$, $-NO_2$, -CN, -COOH, -COOR, -CHO, -COR, -COR, -COR, -F, -CI, -Br, -OH, -OR, -SH, -SR, $-CH=CH_2$, $-CR=CR_2$, and -C=CH.

The substituents may also include those which increase or decrease electronic density in conjugated systems. The former (+R) groups include -CH₃, -CR₃, -F, -Cl, -Br, -I, -OH, -OR, -OCOR, -SH, -SR, -NH₂, -NR₂, and -NHCOR. The later (-R) groups include -NO₂, -CN, -CHC, -COR, -COOH, -COOR, -CONH₂, -SO₂R and -CF₃.

Synthetically speaking, the modifications may be achieved by a variety of unit processes, including nucleophilic and electrophilic substitution, reduction and oxidation, addition elimination, double bond cleavage, and cyclization.

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For the purpose of constructing a library, a compound, or a family of compounds, having one or more pharmacological activities (which need not be related to the known or suspected activities of the target protein), may be disjoined into two or more known or potential pharmacophoric moieties. Analogues of each of these moieties may be identified, and mixtures of these analogues reacted so as to reassemble compounds which have some similarity to the original lead compound. It is not necessary that all members of the library possess moieties analogous to all of the moieties of the lead compound.

The design of a library may be illustrated by the example of the benzodiazepines. Several benzodiazepine drugs, including chlordiazepoxide, diazepam and oxazepam, have been used as anti-anxiety drugs. Derivatives of benzodiazepines have widespread biological activities; derivatives have been reported to act not only as anxiolytics, but also as anticonvul sants; cholecystokinin (CCK) receptor subtype A or B, kappa opioid receptor, platelet activating factor, and HIV transactivator Tat antagonists, and GPIIbIIa, reverse transcriptase and ras farnesyltransferase inhibitors.

The benzodiazepine structure has been disjoined into a 2-aminobenzophenone, an amino acid, and an alkylating agent. See Bunin, et al., Proc. Nat. Acad. Sci. USA, 91:4708 (1994). Since only a few 2-aminobenzophenone derivatives are commercially available, it was later disjoined into 2-aminoarylstannane, an acid chloride, an amino acid, and an alkylating agent. Bunin, et al., Meth. Enzymol., 267:448 (1996). The arylstannane may be considered the core structure upon which the other moieties are substituted, or all four may be considered equals which are conjoined to make each library member.

A basic library synthesis plan and member structure is shown in Figure 1 of Fowlkes, et al_, U.S. Serial No. 08/740,671, incorporated by reference in its entirety. The acid chloride building block introduces variability at the R¹ site. The R² site is introduced by the amino acid, and the R³ site by the alkylating agent. The R⁴ site is inherent in

the arylstannane. Bunin, et al. generated a 1, 4-benzodiazepine library of 11,200 different derivatives prepared from 20 acid chlorides, 35 amino acids, and 16 alkylating agents. (No diversity was introduced at R4; this group was used to couple the molecule to a solid phase.) According to the Available Chemicals Directory (HDL Information Systems, San Leandro CA), over 300 acid chlorides, 80 Fmoc-protected amino acids and 800 alkylating agents were available for purchase (and more, of course, could be synthesized). The particular moieties used were chosen to maximize structural dispersion, while limiting the numbers to those conveniently synthesized in the wells of a microtiter plate. In choosing between structurally similar compounds, preference was given to the least substituted compound.

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The variable elements included both aliphatic and aromatic groups. Among the aliphatic groups, both acyclic and cyclic (mono- or poly-) structures, substituted or not, were tested. (While all of the acyclic groups were linear, it would have been feasible to introduce a branched aliphatic). The aromatic groups featured either single and multiple rings, fused or not, substituted or not, and with heteroatoms or not. The secondary substitutents included - NH₂, -OH, -OMe, -CN, -C1, -F, and -COOH. While not used, spacer moieties, such as -O-, -S-, -OO-, -CS-, -NH-, and -NR-, could have been incorporated.

Bunin et al. suggest that instead of using a 1, 4-benzodiazepine as a core structure, one may instead use a 1, 4-benzodiazepine-2, 5-dione structure.

As noted by Bunin et al., it is advantageous, although not necessary, to use a linkage strategy which leaves no trace of the linking functionality, as this permits construction of a more diverse library.

Other combinatorial nonoligomeric compound libraries known or suggested in the art have been based on carbamates, mercaptoacylated pyrrolidines, phenolic agents, aminimides, N-acylamino ethers (made from amino alcohols, aromatic hydroxy acids, and carboxylic acids), N-alkylamino ethers

WO 2005/082398

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(made from aromatic hydroxy acids, amino alcohols and aldehydes) 1, 4-piperazines, and 1, 4-piperazine-6-ones.

DeWitt, et al., Proc. Nat. Acad. Sci. (USA), 90:6909-13 (1993) describe the simultaneous but separate, synthesis of 40 discrete hydantoins and 40 discrete benzodiazepines. They carry out their synthesis on a solid support (inside a gas dispersion tube), in an array format, as opposed to other conventional simultaneous synthesis techniques (e.g., in a well, or on a pin). The hydantoins were synthesized by first simultaneously deprotecting and then treating each of five amino acid resins with each of eight isocyanates. The benzodiazepines were synthesized by treating each of five deprotected amino acid resins with each of eight 2-amino benzophenone imines.

Chen, et al., J. Am. Chem. Soc., 116:2661-62 (1994) described the preparation of a pilot (9 member) combinatorial library of formate esters. A polymer beadbound aldehyde preparation was "split" into three aliquots, each reacted with one of three different ylide reagents. The reaction products were combined, and then divided into three new aliquots, each of which was reacted with a different Michael donor. Compound identity was found to be determinable on a single bead basis by gas chromatography/mass spectroscopy analysis.

Holmes, USP 5,549,974 (1996) sets forth methodologies for the combinatorial synthesis of libraries of thiazolidinones and metathiazanones. These libraries are made by combination of amines, carbonyl compounds, and thiols under cyclization conditions.

Ellman, USP 5,545,568 (1996) describes combinatorial synthesis of benzodiazepines, prostaglandins, beta-turn mimetics, and glycerol-based compounds. See also Ellman, USP 5,288,514.

Summerton, USP 5,506,337 (1996) discloses methods of preparing a combinatorial library formed predominantly of morpholino subunit structures.

Heterocylic combinatorial libraries are reviewed generally in Nefzi, et al., Chem. Rev., 97:449-472 (1997)

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For pharmacological classes, see, e.g., Goth, Medical Pharmacology: Principles and Concepts (C.V. Mosby Co.: 8th ed. 1976); Korolkovas and Burckhalter, Essentials of Medicinal Chemistry (John Wiley & Sons, Inc.: 1976). For synthetic methods, see, e.g., Warren, Organic Synthesis: The Disconnection Approach (John Wiley & Sons, Ltd.: 1982); Fuson, Reactions of Organic Compounds (John Wiley & Sons: 1966); Payne and Payne, How to do an Organic Synthesis (Allyn and Bacon, Inc.: 1969); Greene, Protective Groups in Organic Synthesis (Wiley-Interscience). For selection of substituents, see e.g., Hansch and Leo, Substituent Constants for Correlation Analysis in Chemistry and Biology (John Wiley & Sons: 1979).

The library is preferably synthesized so that the individual members remain identifiable so that, if a member is shown to be active, it is not necessary to analyze it. Several methods of identification have been proposed, including:

- (1) encoding, i.e., the attachment to each member of an identifier moiety which is more readily identified than the member proper. This has the disadvantage that the tag may itself influence the activity of the conjugate.
- (2) spatial addressing, e.g., each member is synthesized only at a particular coordinate on or in a matrix, or in a particular chamber. This might be, for example, the location of a particular pin, or a particular well on a microtiter plate, or inside a "tea bag".

The present invention is not limited to any particular form of identification.

However, it is possible to simply characterize those members of the library which are found to be active, based on the characteristic spectroscopic indicia of the various building blocks.

Solid phase synthesis permits greater control over which derivatives are formed. However, the solid phase could interfere with activity. To overcome this problem,

some or all of the molecules of each member could be liberated, after synthesis but before screening.

Examples of candidate simple libraries which might be evaluated include derivatives of the following:

Cyclic Compounds Containing One Hetero Atom Heteronitrogen

pyrroles

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pentasubstituted pyrroles

pyrrolidines

pyrrolines

prolines

indoles ·

beta-carbolines

pyridines

15 dihydropyridines

1,4-dihydropyridines

pyrido [2,3-d] pyrimidines

tetrahydro-3H-imidazo[4,5-c] pyridines

Isoquinolines

tetrahydroisoquinolines

quinolones

beta-lactams

azabicyclo[4.3.0]nonen-8-one amino acid

Heterooxygen

furans

tetrahydrofurans

2,5-disubstituted tetrahydrofurans

pyrans

hydroxypyranones

tetrahydroxypyranones

gamma-butyrolactones

Heterosulfur

sulfolenes

Cyclic Compounds with Two or More Hetero atoms

Multiple heteronitrogens

imidazoles

pyrazoles

piperazines

diketopiperazines

arylpiperazines benzylpiperazines

benzodiazepines

1,4-benzodiazepine-2,5-diones

hydantoins

5-alkoxyhydantoins

dihydropyrimidines

1,3-disubstituted-5,6-dihydopyrimidine-2,4-

10 diones

cyclic ureas cyclic thioureas quinazolines

chiral 3-substituted-quinazoline-2,4-

15 diones

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triazoles

1,2,3-triazoles

purines

Heteronitrogen and Heterooxygen

dikelomorpholines

isoxazoles

isoxazolines

Heteronitrogen and Heterosulfur

thiazolidines

N-axylthiazolidines

dihydrothiazoles

2-methylene-2,3-dihydrothiazates

2-aminothiazoles

thiophenes

3-amino thiophenes

4-thiazolidinones

4-melathiazanones

benzisothiazolones ·

For details on synthesis of libraries, see Nefzi, et al., Chem. Rev., 97:449-72 (1997), and references cited therein.

Pharmaceutical Methods and Preparations

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The preferred animal subject of the present invention is a mammal. By the term "mammal" is meant an individual belonging to the class Mammalia. The invention is particularly useful in the treatment of human subjects, although it is intended for veterinary and nutritional uses as well. Preferred nonhuman subjects are of the orders Primata (e.g., apes and monkeys), Artiodactyla or Perissodactyla (e.g., cows, pigs, sheep, horses, goats), Carnivora (e.g., cats, dogs), Rodenta (e.g., rats, mice, guinea pigs, hamsters), Lagomorpha (e.g., rabbits) or other pet, farm or laboratory mammals.

The term "protection", as used herein, is intended to include "prevention," "suppression" and "treatment."

"Prevention", strictly speaking, involves administration of the pharmaceutical prior to the induction of the disease (or other adverse clinical condition). "Suppression" involves administration of the composition prior to the clinical appearance of the disease. "Treatment" involves administration of the protective composition after the appearance of the disease.

It will be understood that in human and veterinary medicine, it is not always possible to distinguish between "preventing" and "suppressing" since the ultimate inductive event or events may be unknown, latent, or the patient is not ascertained until well after the occurrence of the event or events. Therefore, unless qualified, the term "prevention" will be understood to refer to both prevention in the strict sense, and to suppression.

The preventative or prophylactic use of a pharmaceutical usually involves identifying subjects who are at higher risk than the general population of contracting the disease, and administering the pharmaceutical to them in advance of the clinical appearance of the disease. The effectiveness of such use is measured by comparing the subsequent incidence or severity of the disease, or of particular symptoms of the disease, in the treated subjects against that in untreated subjects of the same high risk group.

81

While high risk factors vary from disease to disease, in general, these include (1) prior occurrence of the disease in one or more members of the same family, or, in the case of a contagious disease, in individuals with whom the subject has come into potentially contagious contact at a time when the earlier victim was likely to be contagious, (2) a prior occurrence of the disease in the subject, (3) prior occurrence of a related disease, or a condition known to increase the likelihood of the disease, in the subject; (4) appearance of a suspicious level of a marker of the disease, or a related disease or condition; (5) a subject who is immunologically compromised, e.g., by radiation treatment, HIV infection, drug use,, etc., or (6) membership in a particular group (e.g., a particular age, sex, race, ethnic group, etc.) which has been epidemiologically associated with that disease.

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In some cases, it may be desirable to provide prophylaxis for the general population, and not just a high risk group. This is most likely to be the case when essentially all are at risk of contracting the disease, the effects of the disease are serious, the therapeutic index of the prophylactic agent is high, and the cost of the agent is low.

A prophylaxis or treatment may be curative, that is, directed at the underlying cause of a disease, or ameliorative, that is, directed at the symptoms of the disease, especially those which reduce the quality of life.

It should also be understood that to be useful, the protection provided need not be absolute, provided that it is sufficient to carry clinical value. An agent which provides protection to a lesser degree than do competitive agents may still be of value if the other agents are ineffective for a particular individual, if it can be used in combination with other agents to enhance the level of protection, or if it is safer than competitive agents. It is desirable that there be a statistically significant (p=0.05 or less) improvement in the treated subject relative to an appropriate untreated control, and it is desirable that this improvement be at least 10%, more preferably at least 25%,

PCT/US2005/005596 WO 2005/082398

still more preferably at least 50%, even more preferably at least 100%, in some indicia of the incidence or severity of the disease or of at least one symptom of the disease.

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At least one of the drugs of the present invention may be administered, by any means that achieve their intended purpose, to protect a subject against a disease or other adverse condition. The form of administration may be systemic or topical. For example, administration of such a composition may be by various parenteral routes such as subcutaneous, intravenous, intradermal, intramuscular, intraperitoneal, intranasal, transdermal, or buccal routes. Alternatively, or concurrently, administration may be by the oral route. Parenteral administration can be by bolus injection or by gradual perfusion over time.

A typical regimen comprises administration of an effective amount of the drug, administered over a period ranging from a single dose, to dosing over a period of hours, days, weeks, months, or years.

It is understood that the suitable dosage of a drug of the present invention will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired. However, the most preferred dosage can be tailored to the individual subject, as is understood and determinable by one of skill in the art, without undue experimentation. This will typically involve adjustment of a standard dose, e.g., reduction of the dose if the patient has a low body weight.

Prior to use in humans, a drug will first be evaluated for safety and efficacy in laboratory animals. In human clinical studies, one would begin with a dose expected to be safe in humans, based on the preclinical data for the drug in question, and on customary doses for analogous drugs (if If this dose is effective, the dosage may be decreased, to determine the minimum effective dose, if desired. If this dose is ineffective, it will be cautiously increased, with the patients monitored for signs of side effects. See, e.g., Berkow et al, eds., The Merck Manual, 15th edition, Merck and Co., Rahway, N.J., 1987; Goodman et

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al., eds., Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th edition, Pergamon Press, Inc., Elmsford, N.Y., (1990); Avery's Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987), Ebadi, Pharmacology, Little, Brown and Co., Boston, (1985), which references and references cited therein, are entirely incorporated herein by reference.

The total dose required for each treatment may be administered by multiple doses or in a single dose. The protein may be administered alone or in conjunction with other therapeutics directed to the disease or directed to other symptoms thereof.

Typical pharmaceutical doses, for adult humans, are in the range of 1 ng to 10g per day, more often 1 mg to 1g per day.

The appropriate dosage form will depend on the disease, the pharmaceutical, and the mode of administration; possibilities include tablets, capsules, lozenges, dental pastes, suppositories, inhalants, solutions, ointments and parenteral depots. See, e.g., Berker, supra, Goodman, supra, Avery, supra and Ebadi, supra, which are entirely incorporated herein by reference, including all references cited therein.

In the case of peptide drugs, the drug may be administered in the form of an expression vector comprising a nucleic acid encoding the peptide; such a vector, after incorporation into the genetic complement of a cell of the patient, directs synthesis of the peptide. Suitable vectors include genetically engineered poxviruses (vaccinia), adenoviruses, adeno-associated viruses, herpesviruses and lentiviruses which are or have been rendered nonpathogenic.

In addition to at least one drug as described herein, a pharmaceutical composition may contain suitable pharmaceutically acceptable carriers, such as excipients, carriers and/or auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. See, e.g., Berker, supra, Goodman, supra, Avery, supra and Ebadi, supra, which are entirely

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incorporated herein by reference, included all references cited therein.

Assay Compositions and Methods

Target Organism

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The invention contemplates that it may be appropriate to ascertain or to mediate the biological activity of a substance of this invention in a target organism.

The target organism may be a plant, animal, or microorganism.

In the case of a plant, it may be an economic plant, in which case the drug may be intended to increase the disease, weather or pest resistance, alter the growth characteristics, or otherwise improve the useful characteristics or mute undesirable characteristics of the plant. Or it may be a weed, in which case the drug may be intended to kill or otherwise inhibit the growth of the plant, or to alter its characteristics to convert it from a weed to an economic plant. The plant may be a tree, shrub, crop, grass, etc. The plant may be an algae (which are in some cases also microorganisms), or a vascular plant, especially gymnosperms (particularly conifers) and angiosperms. Angiosperms may be monocots or dicots. plants of greatest interest are rice, wheat, corn, alfalfa, soybeans, potatoes, peanuts, tomatoes, melons, apples, pears, plums, pineapples, fir, spruce, pine, cedar, and oak.

If the target organism is a microorganism, it may be algae, bacteria, fungi, or a virus (although the biological activity of a virus must be determined in a virus-infected cell). The microorganism may be human or other animal or plant pathogen, or it may be nonpathogenic. It may be a soil or water organism, or one which normally lives inside other living things.

If the target organism is an animal, it may be a vertebrate or a nonvertebrate animal. Nonvertebrate animals are chiefly of interest when they act as pathogens or parasites, and the drugs are intended to act as biocidic or biostatic agents. Nonvertebrate animals of interest include worms, mollusks, and arthropods.

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The target organism may also be a vertebrate animal, i.e., a mammal, bird, reptile, fish or amphibian. Among mammals, the target animal preferably belongs to the order Primata (humans, apes and monkeys), Artiodactyla (e.g., cows, pigs, sheep, goats, horses), Rodenta (e.g., mice, rats) Lagomorpha (e.g., rabbits, hares), or Carnivora (e.g., cats, dogs). Among birds, the target animals are preferably of the orders Anseriformes (e.g., ducks, geese, swans) or Galliformes (e.g., quails, grouse, pheasants, turkeys and chickens). Among fish, the target animal is preferably of the order Clupeiformes (e.g., sardines, shad, anchovies, whitefish, salmon).

Target Tissues

The term "target tissue" refers to any whole animal, physiological system, whole organ, part of organ, miscellaneous tissue, cell, or cell component (e.g., the cell membrane) of a target animal in which biological activity may be measured.

Routinely in mammals one would choose to compare and contrast the biological impact on virtually any and all tissues which express the subject receptor protein. The main tissues to use are: brain, heart, lung, kidney, liver, pancreas, skin, intestines, adipose, stomach, skeletal muscle, adrenal glands, breast, prostate, vasculature, retina, cornea, thyroid gland, parathyroid glands, thymus, bone marrow, bone, etc.

Another classification would be by cell type: B cells, T cells, macrophages, neutrophils, eosinophils, mast cells, platelets, megakaryocytes, erythrocytes, bone marrow stomal cells, fibroblasts, neurons, astrocytes, neuroglia, microglia, epithelial cells (from any organ, e.g. skin, breast, prostate, lung, intestines etc), cardiac muscle cells, smooth muscle cells, striated muscle cells, osteoblasts, osteocytes, chondroblasts, chondrocytes, keratinocytes, melanocytes, etc.

Of course, in the case of a unicellular organism, there is no distinction between the "target organism" and the "target tissue".

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Screening Assays

Assays intended to determine the binding or the biological activity of a substance are called preliminary screening assays.

Screening assays will typically be either in vitro (cell-free) assays (for binding to an immobilized receptor) or cell-based assays (for alterations in the phenotype of the cell). They will not involve screening of whole multicellular organisms, or isolated organs. The comments on diagnostic biological assays apply mutatis mutandis to screening cell-based assays.

In Vitro vs. In Vivo Assays

The term in vivo is descriptive of an event, such as binding or enzymatic action, which occurs within a living organism. The organism in question may, however, be genetically modified. The term in vitro refers to an event which occurs outside a living organism. Parts of an organism (e.g., a membrane, or an isolated biochemical) are used, together with artificial substrates and/or conditions. For the purpose of the present invention, the term in vitro excludes events occurring inside or on an intact cell, whether of a unicellular or multicellular organism.

In vivo assays include both cell-based assays, and organismic assays. The cell-based assays include both assays on unicellular organisms, and assays on isolated cells or cell cultures derived from multicellular organisms. The cell cultures may be mixed, provided that they are not organized into tissues or organs. The term organismic assay refers to assays on whole multicellular organisms, and assays on isolated organs or tissues of such organisms.

In vitro Diagnostic Methods and Reagents

The in vitro assays of the present invention may be applied to any suitable analyte-containing sample, and may be qualitative or quantitative in nature.

Sample

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The sample will normally be a biological fluid, such as blood, urine, lymph, semen, milk, or cerebrospinal fluid, or a fraction or/derivative thereof, or a biological tissue, in the form of, e.g., a tissue section or homogenate. However, the sample conceivably could be (or derived from) a food or beverage, a pharmaceutical or diagnostic composition, soil, or surface or ground water. If a biological fluid or tissue, it may be taken from a human or other mammal, vertebrate or animal, or from a plant. The preferred sample is blood, or a fraction or derivative thereof.

Binding and Reaction Assays

The assay may be a binding assay, in which one step involves the binding of a diagnostic reagent to the analyte, or a reaction assay, which involves the reaction of a reagent with the analyte. The reagents used in a binding assay may be classified as to the nature of their interaction with analyte: (1) analyte analogues, or (2) analyte binding molecules (ABM). They may be labeled or insolubilized.

In a reaction assay, the assay may look for a direct reaction between the analyte and a reagent which is reactive with the analyte, or if the analyte is an enzyme or enzyme inhibitor, for a reaction catalyzed or inhibited by the analyte. The reagent may be a reactant, a catalyst, or an inhibitor for the reaction.

An assay may involve a cascade of steps in which the product of one step acts as the target for the next step. These steps may be binding steps, reaction steps, or a combination thereof.

Signal Producing System (SPS)

In order to detect the presence, or measure the amount, of an analyte, the assay must provide for a signal producing system (SPS) in which there is a detectable difference in the signal produced, depending on whether the analyte is present or absent (or, in a quantitative assay, on the

amount of the analyte). The detectable signal may be one which is visually detectable, or one detectable only with instruments. Possible signals include production of colored or luminescent products, alteration of the characteristics (including amplitude or polarization) of absorption or emission of radiation by an assay component or product, and precipitation or agglutination of a component or product. The term "signal" is intended to include the discontinuance of an existing signal, or a change in the rate of change of an observable parameter, rather than a change in its absolute value. The signal may be monitored manually or automatically.

In a reaction assay, the signal is often a product of the reaction. In a binding assay, it is normally provided by a label borne by a labeled reagent.

Labels

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The component of the signal producing system which is most intimately associated with the diagnostic reagent is called the "label". A label may be, e.g., a radioisotope, a fluorophore, an enzyme, a co-enzyme, an enzyme substrate, an electron-dense compound, an agglutinable particle.

The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography. Isotopes which are particularly useful for the purpose of the present invention include ³H, ¹²⁵I, ¹³¹I, ³⁵S, ¹⁴C, ³²P and ³³P. ¹²⁵I is preferred for antibody labeling.

The label may also be a fluorophore. When the fluorescently labeled reagent is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycocrythrin, phycocyanin, allophycocyanin, ophthaldehyde and fluorescamine.

Alternatively, fluorescence-emitting metals such as ¹²⁵Eu, or others of the lanthanide series, may be incorporated into a diagnostic reagent using such metal

chelating groups as diethylenetriaminepentaacetic acid (DTPA) of ethylenediamine-tetraacetic acid (EDTA).

The label may also be a chemiluminescent compound. presence of the chemiluminescently labeled reagent is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. of particularly useful chemiluminescent labeling compounds are luminol, isolumino, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used for Bioluminescence is a type of chemiluminescence, found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. 'Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Enzyme labels, such as horseradish peroxidase and alkaline phosphatase, are preferred. When an enzyme label is used, the signal producing system must also include a substrate for the enzyme. If the enzymatic reaction product is not itself detectable, the SPS will include one or more additional reactants so that a detectable product appears.

An enzyme analyte may act as its own label if an enzyme inhibitor is used as a diagnostic reagent.

Binding Assay Formats

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Binding assays may be divided into two basic types, heterogeneous and homogeneous. In heterogeneous assays, the interaction between the affinity molecule and the analyte does not affect the label, hence, to determine the amount or presence of analyte, bound label must be separated from free In homogeneous assays, the interaction does affect label. the activity of the label, and therefore analyte levels can be deduced without the need for a separation step.

In one embodiment, the ABM is insolubilized by coupling it to a macromolecular support, and analyte in the sample is allowed to compete with a known quantity of a labeled or specifically labelable analyte analogue. The "analyte

WO 2005/082398

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analogue" is a molecule capable of competing with analyte for binding to the ABM, and the term is intended to include analyte itself. It may be labeled already, or it may be labeled subsequently by specifically binding the label to a moiety differentiating the analyte analogue from analyte. The solid and liquid phases are separated, and the labeled analyte analogue in one phase is quantified. The higher the level of analyte analogue in the solid phase, i.e., sticking to the ABM, the lower the level of analyte in the sample.

In a "sandwich assay", both an insolubilized ABM, and a labeled ABM are employed. The analyte is captured by the insolubilized ABM and is tagged by the labeled ABM, forming a ternary complex. The reagents may be added to the sample in either order, or simultaneously. The ABMs may be the same or different. The amount of labeled ABM in the ternary complex is directly proportional to the amount of analyte in the sample.

The two embodiments described above are both heterogeneous assays. However, homogeneous assays are conceivable. The key is that the label be affected by whether or not the complex is formed. Conjugation Methods

A label may be conjugated, directly or indirectly (e.g., through a labeled anti-ABM antibody), covalently (e.g., with SPDP) or noncovalently, to the ABM, to produce a diagnostic reagent. Similarly, the ABM may be conjugated to a solid phase support to form a solid phase ("capture") diagnostic reagent.

Suitable supports include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention.

The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to its target. Thus the support configuration may be spherical, as in a bead, or

cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc.

5 <u>Biological Assays</u>

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A biological assay measures or detects a biological response of a biological entity to a substance.

The biological entity may be a whole organism, an isolated organ or tissue, freshly isolated cells, an immortalized cell line, or a subcellular component (such as a membrane; this term should not be construed as including an isolated receptor). The entity may be, or may be derived from, an organism which occurs in nature, or which is modified in some way. Modifications may be genetic (including radiation and chemical mutants, and genetic engineering) or somatic (e.g., surgical, chemical, etc.). In the case of a multicellular entity, the modifications may affect some or all cells. The entity need not be the target organism, or a derivative thereof, if there is a reasonable correlation between bioassay activity in the assay entity and biological activity in the target organism.

The entity is placed in a particular environment, which may be more or less natural. For example, a culture medium may, but need not, contain serum or serum substitutes, and it may, but need not, include a support matrix of some kind, it may be still, or agitated. It may contain particular biological or chemical agents, or have particular physical parameters (e.g., temperature), that are intended to nourish or challenge the biological entity.

There must also be a detectable biological marker for the response. At the cellular level, the most common markers are cell survival and proliferation, cell behavior (clustering, motility), cell morphology (shape, color), and biochemical activity (overall DNA synthesis, overall protein synthesis, and specific metabolic activities, such as utilization of particular nutrients, e.g., consumption of oxygen, production of CO₂, production of organic acids, uptake or discharge of ions).

92

The direct signal produced by the biological marker may be transformed by a signal producing system into a different signal which is more observable, for example, a fluorescent or colorimetric signal.

The entity, environment, marker and signal producing system are chosen to achieve a clinically acceptable level of sensitivity, specificity and accuracy.

In some cases, the goal will be to identify substances which mediate the biological activity of a natural biological entity, and the assay is carried out directly with that entity. In other cases, the biological entity is used simply as a model of some more complex (or otherwise inconvenient to work with) biological entity. In that event, the model biological entity is used because activity in the model system is considered more predictive of activity in the ultimate natural biological entity than is simple binding activity in an in vitro system. The model entity is used instead of the ultimate entity because the former is more expensive or slower to work with, or because ethical considerations forbid working with the ultimate entity yet.

The model entity may be naturally occurring, if the model entity usefully models the ultimate entity under some conditions. Or it may be non-naturally occurring, with modifications that increase its resemblance to the ultimate entity.

Transgenic animals, such as transgenic mice, rats, and rabbits, have been found useful as model systems.

In cell-based model assays, where the biological activity is mediated by binding to a receptor (target protein), the receptor may be functionally connected to a signal (biological marker) producing system, which may be endogenous or exogenous to the cell.

There are a number of techniques of doing this.

"Zero-Hybrid": Systems

WO 2005/082398

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In these systems, the binding of a peptide to the target protein results in a screenable or selectable phenotypic change, without resort to fusing the target

PCT/US2005/005596 WO 2005/082398

93

protein (or a ligand binding moiety thereof) to an endogenous protein. It may be that the target protein is endogenous to the host cell, or is substantially identical to an endogenous receptor so that it can take advantage of the latter's native signal transduction pathway. sufficient elements of the signal transduction pathway normally associated with the target protein may be engineered into the cell so that the cell signals binding to the target protein.

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"One-Hybrid" Systems

In these systems, a chimera receptor, a hybrid of the target protein and an endogenous receptor, is used. chimeric receptor has the ligand binding characteristics of the target protein and the signal transduction characteristics of the endogenous receptor. Thus, the normal signal transduction pathway of the endogenous receptor is subverted.

Preferably, the endogenous receptor is inactivated, or the conditions of the assay avoid activation of the endogenous receptor, to improve the signal-to-noise ratio.

See Fowlkes USP 5,789,184 for a yeast system.

Another type of "one-hybrid" system combines a peptide: DNA-binding domain fusion with an unfused target receptor that possesses an activation domain.

"Two-Hybrid" System

In a preferred embodiment, the cell-based assay is a two hybrid system. This term implies that the ligand is incorporated into a first hybrid protein, and the receptor into a second hybrid protein. The first hybrid also comprises component A of a signal generating system, and the second hybrid comprises component B of that system. Components A and B, by themselves, are insufficient to generate a signal. However, if the ligand binds the receptor, components A and B are brought into sufficiently close proximity so that they can cooperate to generate a signal.

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Components A and B may naturally occur, or be substantially identical to moieties which naturally occur, as components of a single naturally occurring biomolecule, or they may naturally occur, or be substantially identical to moieties which naturally occur, as separate naturally occurring biomolecules which interact in nature.

Two-Hybrid System: Transcription Factor Type

In a preferred "two-hybrid" embodiment, one member of a peptide ligand:receptor binding pair is expressed as a fusion to a DNA-binding domain (DBD) from a transcription factor (this fusion protein is called the "bait"), and the other is expressed as a fusion to a transactivation domain (TAD) (this fusion protein is called the "fish", the "prey", or the "catch"). The transactivation domain should be complementary to the DNA-binding domain, i.e., it should interact with the latter so as to activate transcription of a specially designed reporter gene that carries a binding site for the DNA-binding domain. Naturally, the two fusion proteins must likewise be complementary.

This complementarity may be achieved by use of the complementary and separable DNA-binding and transcriptional activator domains of a single transcriptional activator protein, or one may use complementary domains derived from different proteins. The domains may be identical to the native domains, or mutants thereof. The assay members may be fused directly to the DBD or TAD, or fused through an intermediated linker.

The target DNA operator may be the native operator sequence, or a mutant operator. Mutations in the operator may be coordinated with mutations in the DBD and the TAD. An example of a suitable transcription activation system is one comprising the DNA-binding domain from the bacterial repressor LexA and the activation domain from the yeast transcription factor Gal4, with the reporter gene operably linked to the LexA operator.

It is not necessary to employ the intact target receptor; just the ligand-binding moiety is sufficient.

WO 2005/082398

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The two fusion proteins may be expressed from the same or different vectors. Likewise, the activatable reporter gene may be expressed from the same vector as either fusion protein (or both proteins), or from a third vector.

Potential DNA-binding domains include Gal4, LexA, and mutant domains substantially identical to the above.

Potential activation domains include E. coli B42, Gal4 activation domain II, and HSV VP16, and mutant domains substantially identical to the above.

Potential operators include the native operators for the desired activation domain, and mutant domains substantially identical to the native operator.

The fusion proteins may comprise nuclear localization signals.

The assay system will include a signal producing system, too. The first element of this system is a reporter gene operably linked to an operator responsive to the DBD and TAD of choice. The expression of this reporter gene will result, directly or indirectly, in a selectable or screenable phenotype (the signal). The signal producing system may include, besides the reporter gene, additional genetic or biochemical elements which cooperate in the production of the signal. Such an element could be, for example, a selective agent in the cell growth medium. There may be more than one signal producing system, and the system may include more than one reporter gene.

The sensitivity of the system may be adjusted by, e.g., use of competitive inhibitors of any step in the activation or signal production process, increasing or decreasing the number of operators, using a stronger or weaker DBD or TAD, etc.

When the signal is the death or survival of the cell in question, or proliferation or monproliferation of the cell in question, the assay is said to be a selection. When the signal merely results in a detectable phenotype by which the signaling cell may be differentiated from the same cell in a nonsignaling state (either way being a living cell), the assay is a screen. However, the term "screening assay" may be used in a broader sense to include a selection. When the

narrower sense is intended, we will use the term "nonselective screen".

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Various screening and selection systems are discussed in Ladner, USP 5,198,346.

Screening and selection may be for or against the peptide: target protein or compound:target protein interaction.

Preferred assay cells are microbial (bacterial, yeast, algal, protozooal), invertebrate, vertebrate (esp. mammalian, particularly human). The best developed twohybrid assays are yeast and mammalian systems.

Normally, two hybrid assays are used to determine whether a protein X and a protein Y interact, by virtue of their ability to reconstitute the interaction of the DBD and the TAD. However, augmented two-hybrid assays have been used to detect interactions that depend on a third, nonprotein ligand.

For more guidance on two-hybrid assays, see Brent and Finley, Jr., Ann. Rev. Genet., 31:663-704 (1997); Fremont-Racine, et al., Nature Genetics, 277-281 (16 July 1997); Allen, et al., TIBS, 511-16 (Dec. 1995); LeCrenier, et al., BioEssays, 20:1-6 (1998); Xu, et al., Proc. Nat. Acad. sci. (USA), 94:12473-8 (Nov. 1992); Esotak, et al., Mol. Cell. Biol., 15:5820-9 (1995); Yang, et al., Nucleic Acids Res., 23:1152-6 (1995); Bendixen, et al., Nucleic Acids Res., 22:1778-9 (1994); Fuller, et al., BioTechniques, 25:85-92 (July 1998); Cohen; et al., PNAS (USA) 95:14272-7 (1998); Kolonin and Finley, Jr., PNAS (USA) 95:14266-71 (1998). also Vasavada, et al., PNAS (USA), 88:10686-90 (1991) (contingent replication assay), and Rehrauer, et al., J. Biol. Chem., 271:23865-73 91996) (LexA repressor cleavage assay).

Two-Hybrid Systems: reporter Enzyme type

In another embodiment, the components A and B reconstitute an enzyme which is not a transcription factor.

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As in the last example, the effect of the reconstitution of the enzyme is a phenotypic change which may be a screenable change, a selectable change, or both.

5 <u>In vivo Diagnostic Uses</u>

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Radio-labeled ABM may be administered to the human or animal subject. Administration is typically by injection, e.g., intravenous or arterial or other means of administration in a quantity sufficient to permit subsequent dynamic and/or static imaging using suitable radio-detecting devices. The dosage is the smallest amount capable of providing a diagnostically effective image, and may be determined by means conventional in the art, using known radio-imaging agents as a guide.

Typically, the imaging is carried out on the whole body of the subject, or on that portion of the body or organ relevant to the condition or disease under study. The amount of radio-labeled ABM accumulated at a given point in time in relevant target organs can then be quantified.

A particularly suitable radio-detecting device is a scintillation camera, such as a gamma camera. A scintillation camera is a stationary device that can be used to image distribution of radio-labeled ABM. The detection device in the camera senses the radioactive decay, the distribution of which can be recorded. Data produced by the imaging system can be digitized. The digitized information can be analyzed over time discontinuously or continuously. The digitized data can be processed to produce images, called frames, of the pattern of uptake of the radio-labeled ABM in the target organ at a discrete point in time. most continuous (dynamic) studies, quantitative data is obtained by observing changes in distributions of radioactive decay in target organs over time. In other words, a time-activity analysis of the data will illustrate uptake through clearance of the radio-labeled binding protein by the target organs with time.

Various factors should be taken into consideration in selecting an appropriate radioisotope. The radioisotope must be selected with a view to obtaining good quality

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resolution upon imaging, should be safe for diagnostic use in humans and animals, and should preferably have a short physical half-life so as to decrease the amount of radiation received by the body. The radioisotope used should preferably be pharmacologically inert, and, in the quantities administered, should not have any substantial physiological effect.

The ABM may be radio-labeled with different isotopes of iodine, for example ¹²³I, ¹²⁵I, or ¹³¹I (see for example, U.S. Patent 4,609,725). The extent of radio-labeling must, however be monitored, since it will affect the calculations made based on the imaging results (i.e. a diiodinated ABM will result in twice the radiation count of a similar monoiodinated ABM over the same time frame).

In applications to human subjects, it may be desirable to use radioisotopes other than ¹²⁵I for labeling in order to decrease the total dosimetry exposure of the human body and to optimize the detectability of the labeled molecule (though this radioisotope can be used if circumstances require). Ready availability for clinical use is also a factor. Accordingly, for human applications, preferred radio-labels are for example, ^{99m}Tc, ⁶⁷Ga, ⁶⁸Ga, ⁹⁰Y, ¹¹¹In, ^{113m}In, ¹²³I, ¹⁸⁶Re, ¹⁸⁸Re or ²¹¹At.

The radio-labeled ABM may be prepared by various methods. These include radio-halogenation by the chloramine - T method or the lactoperoxidase method and subsequent purification by HPLC (high pressure liquid chromatography), for example as described by J. Gutkowska et al in "Endocrinology and Metabolism Clinics of America: (1987) 16 (1):183. Other known methods of radio-labeling can be used, such as IODOBEADS™.

There are a number of different methods of delivering the radio-labeled ABM to the end-user. It may be administered by any means that enables the active agent to reach the agent's site of action in the body of a mammal. Because proteins are subject to being digested when administered orally, parenteral administration, i.e., intravenous, subcutaneous, intramuscular, would ordinarily

PCT/US2005/005596 WO 2005/082398

99 be used to optimize absorption of an ABM, such as an antibody, which is a protein.

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EXAMPLES

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We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat and has been documented to lead to diabetes in C57BL/6J mice (Surwit at al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets. At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. For further analysis, RNA was extracted from the gastrocnemius muscles at each time point and used in DNA microarray analyses.

15 Animal Models.

Obesity and subsequent hyperinsulinemia and hyperglycemia were induced by feeding a group of 3 week old mice (50 C57BL/6 males) a high-fat diet (Bio-Serve, Frenchtown, NJ, #F1850 High Carbohydrate-High Fat; 56% of calories from fat, 16% from protein and 27% from carbohydrates): Another group of 3 week old mice (20 C57B1/6 males) were fed the normal control diet (PMI Nutrition International Inc., Brentwood, MO, Prolab RMH3000; 14% of calories from fat, 16% from protein and 60% from carbohydrates). The mice were placed onto the respective diets immediately following weaning. Animal weights were determined weekly. Fasting blood-glucose and plasma insulin measurements were determined after 2, 4, 8 and 16 weeks on the respective diets.

The day after obtaining body weight measurements at the indicated time points, mice were fasted 8 hours and blood glucose concentrations were measured via tail blood samples using a One Touch Glucometer (Lifescan). For insulin measurements, blood was collected into heparinized tubes, plasma obtained by centrifugation and insulin concentrations determined using an Ultra-Sensitive Rat Insulin ELISA kit (ALPCO) as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for species difference in cross-

101

reactivity with the antibody (bottom panel). Results reflect mean \pm SE of 50 mice on the HF diet and 20 mice on the Std diet.

Normal weight, normal fasting blood glucose and normal fasting plasma insulin levels are defined as the respective mean values of the animals fed the control diet.

Two of the "most typical" animals were selected for each group (Control, hyperinsulinemic and Diabetic) at each time point (2,4,8, and 16 weeks after commencement of diet) for sacrifice. The selected mice were sacrificed and muscle tissue obtained and immediately processed for RNA isolation.

Fasting Blood Glucose Levels.

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Blood glucose levels was measured from a drop of blood taken from the tip of the tail of fasted (8 hr) mice using a Lifescan Genuine One Touch glucometer. All measurements occurred between 2:00 pm and 5:00 pm.

Plasma insulin measurements.

Blood was collected from the tail of fasted (8 hr) mice into a heparinized capillary tube and stored on ice. All collections occurred between 2:00 pm and 5:00 pm. Plasma was separated from red blood cells by centrifugation for 10 minutes at 8000 x g and then stored at -20°C. Insulin concentrations were determined using the Rat Insulin ELISA kit and rat insulin standards (ALPCO) essentially as instructed by the manufacturer. Values were adjusted by a factor of 1.23 as determined by the manufacturer to correct for the species difference in cross-reactivity with the antibody.

RNA isolation.

Total RNA was isolated from muscle (skeletal muscle, specifically, gastrocnemius) of two mice at each time point during the progression of HF diet-induced type 2 diabetes, as well as age-matched controls on the Std diet, using the RNA STAT-60 Total RNA/mRNA Isolation Reagent according to the manufacturer's instructions (Tel-Test, Friendswood, TX).

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Sample Quantification and Quality Assessment

Total RNA was quantified and assessed for quality on a Bioanalyzer RNA 6000 Nano chip (Agilent). Each chip contained an interconnected set of gel-filled channels that allowed for molecular sieving of mucleic acids. Pinelectrodes in the chip were used to create electrokinetic forces capable of driving molecules through these microchannels to perform electrophoretic separations. Ribosomal peaks were measured by fluorescence signal and displayed in an electropherogram. A successful total RNA sample featured 2 distinct ribosomal peaks (18S and 28S rRNA).

Biotinylated cRNA Hybridization Target.

Total RNA was prepared for use as a hybridization target as described in the manufacturer's instructions for CodeLink Expression Bioarrays (TM) (Amersham Biosciences). The CodeLink Expression Bioarrays utilize nucleic acid hybridization of a biotin-labeled complementary RNA(cRNA) target with DNA oligonucleotide probes attached to a gel matrix.

The biotin-labeled cRNA target is prepared by a linear amplification method. Poly (A) + RNA (within the total RNA population) is primed for reverse transcription by a DNA oligonucleotide containing a T7 RNTA polymerase promoter 5' to a (dT) 24 sequence. After second-strand cDNA synthesis, the cDNA serves as the template in an in vitro transcription (IVT) reaction to produce the target cRNA. The IVT is performed in the presence of biotinylated nucleotides to label the target cRNA. This procedure results in a 50-200 fold linear amplification of the input poly (A) + RNA.

Hybridization Probes.

The oligonucleotide probes were provided by the Codelink Uniset Mouse I Bioarray (Amersham, product code 300013). Amine-terminated oligonucleotide probes are attached to a three-dimensional polyacrylamide gel matrix. There are 10,000 oligonucleotide probes, each specific to a well-characterized mouse gene. Each mouse gene is

representative of a unique gene cluster from the fourth quarter 2001 Genbank Unigene build. There are also 500 control probes.

The sequences of the probes are proprietary to

Amersham. However, for each probe, Amersham identifies the corresponding mouse gene by NCBI accession number, OGS,
LocusLink, Unigene Cluster ID, and description (name).

This information should be available from Amersham. In the case of the differentially expressed probes, this information is duplicated in master table 1. For the complete list, see

http://www4.amershambiosciences.com/aptrix/upp01077.nsf/Content/codelink_literature

15 Under "Gene Lists", select "Uniset Mouse I", and a gene list, in Excel format, can be downloaded.

Hybridization

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Using the cRNA target, the hybridization reaction mixture is prepared and loaded into array chambers for bioarray processing as set forth in the manufacturer's instructions for CodeLink Gene Expression BioarraysTM (Amerhsam Biosciences). Each sample is hybridized to an individual microarray. Hybridization is at 37°C. The hybridization buffer is prepared as set forth in the Motorola instructions. Hybridization to the microarray is detected with an avidinated fluorescent reagent, Streptavidin-Alexa Fluor [®] 647 (Amersham).

Mouse Gene Expression Analysis

Processed arrays were scanned using a GenePix 4000B Microarray Scanner (Axon Instruments, Inc.); array images were acquired using the Amersham CodeLink™ Analysis Software (Release 2.2). The Amersham CodeLink™ Analysis Software gives an integrated optical density (IOD) value for every spot; a unique background value for that spot is subtracted, resulting in "raw" data points. Individual chips are then normalized by the Amersham Codelink™ software according to the median raw intensity for all 10,000 genes. A negative

WO 2005/082398

control threshold (0.2) is also calculated according to the control probes. The expression data was analyzed to identify genes whose expression levels changed significantly with respect to:

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Normal mice compared to hyperinsulinemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

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Normal mice compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on normal vs. high-fat diet.

Hyperinsulinemic compared to hyperinsulinemic/hyperglycemic mice at 2, 4, 8 and 16 weeks on high-fat diets.

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Database Searches Nucleotide sequences and predicted amino acid sequences were compared to public domain databases using the Blast 2.0 program (National Center for Biotechnology Information, National Institutes of Health). Nucleotide sequences were displayed using ABI prism Edit View 1.0.1 (PE Applied Biosystems, Foster City, CA).

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Nucleotide database searches were conducted with the then current version of BLASTN 2.0.12, see Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res., 25:3389-3402 Searches employed the default parameters, unless otherwise stated.

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For blastN searches, the default was the blastN matrix (1,-3), with gap penalties of 5 for existence and 2 for extension.

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Protein database searches were conducted with the thencurrent version of BLAST X, see Altschul et al. (1997); supra. Searches employed the default parameters, unless otherwise stated. The scoring matrix was BLOSUM62, with gap costs of 11 for existence and 1 for extension. The standard low complexity filter was used.

"ref" indicates that NCBI's RefSeq is the source : database. The identifier that follows is a RefSeq accession

105

number, not a GenBank accession number. "RefSeq sequences are derived from GenBank and provide non-redundant curated data representing our current knowledge of known genes. Some records include additional sequence information that was never submitted to an archival database but is available in the literature. A small number of sequences are provided through collaboration; the underlying primary sequence data is available in GenBank, but may not be available in any one GenBank record. RefSeq sequences are not submitted primary sequences. RefSeq records are owned by NCBI and therefore can be updated as needed to maintain current annotation or to incorporate additional sequence information." See also http://www.ncbi.nlm.nih.gov/LocusLink/refseq.html

It will be appreciated by those in the art that the exact results of a database search will change from day to day, as new sequences are added. Also, if you query with a longer version of the original sequence, the results will change. The results given here were obtained at one time and no guarantee is made that the exact same hits would be obtained in a search on the filing date. However, if an alignment between a particular query sequence and a particular database sequence is discussed, that alignment should not change (if the parameters and sequences remain unchanged).

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Northern Analysis.

Northern analysis may be used to confirm the results. Favorable and unfavorable genes, identified as described above, or fragments thereof, will be used as probes in Northern hybridization analyses to confirm their differential expression. Total RNA isolated from subject mice will be resolved by agarose gel electrophoresis through a 1% agarose, 1 % formaldehyde denaturing gel, transferred to positively charged nylon membrane, and hybridized to a probe labeled with [32P] dCTP that was generated from the aforementioned gene or fragment using the Random Primed DNA Labeling Kit (Roche, Palo Alto, CA), or to a probe labeled with digoxigenin (Roche Molecular Biochemicals,

106

Indianapolis, IN), according to the manufacturer's instructions.

Real-Time RNA Analysis.

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Real-time RNA analysis may also be used for confirmation. For "real-time" RNA analysis, RNA will be converted to cDNA and then probed with gene-specific primers made for each clone. "Real-time" incorporation of fluorescent dye will be measured to determine the amount of specific transcript present in each sample. Sample differences (control vs. hyperinsulinemic, hyperinsulinemic vs. diabetic, or control vs. diabetic) will be evaluated. Confirmation using several independent animals is desirable.

15 In situ Hybridization

Another form of confirmation may be provided by nonisotopic in situ hybridizations (NISH) on selected human (obtained by Tissue Informatics) and mouse tissues using cRNA probes generated from mouse genes found to be up- or . 20 down-regulated during the disease progression. hybridizations may also be performed on mouse tissues using cRNA probes generated from differentially expressed DNAs. These cRNA's will hybridize to their corresponding messenger RNA's present in cells and will provide information regarding the particular cell types within a tissue that is 25 . expressing the particular gene as well as the relative level of gene expression. The cRNA probes may be generated by in vitro transcription of template cDNA by Sp6 or T7 RNA polymerase in the presence of digoxigenin-11-UTP (Roche Molecular Biochemicals, Mannheim, Germany; Pardue, M.L. 30 In: In situ hybridization, Nucleic acid hybridization, a practical approach: IRL Press, Oxford, 179-202).

35 Transgenic Animals.

Transgenic expression may be used to confirm the results. In one embodiment, a mouse is engineered to overexpress the favorable or unfavorable mouse gene in question. In another embodiment, a mouse is engineered to express the

corresponding favorable or unfavorable human gene. third embodiment, a nonhuman animal other than a mouse, such as a rat, rabbit, goat, sheep or pig, is engineered to express the favorable or unfavorable mouse or human gene.

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Hyperquantitative Tissue Analysis

In addition to gene expression analysis the tissue sections can also be analyzed using TissueInformatics, Inc.'s TissueAnalytics™ software. A single representative section may be cut from each tissue block, placed on a slide, and stained with H&E. Digital images of each slide may be acquired using an research microscope and digital camera (Olympus E600 microscope and Sony DKC-ST5). These images may be acquired at 20x magnification with a resolution of 0.64 mm/pixel. A hyperquantitative analysis may be performed on the resulting images: First a digital image analysis can identify and annotate structural objects in a tissue using machine vision. These objects, which are constituents of the tissue, can be annotated because they are visually identifiable and have a biological meaning. Subsequently a quantification of these structures regarding: their geometric properties like area or stain intensities and their relationship to the field of view or per unit area. in terms of a % coverage may be performed. Features or parameters for hyper-quantification are specific for each tissue, and may also include relations between features, measures of overall heterogeneity, including orientation, relative locations, and textures.

.30 Correlation Analysis

Mathematical statistics provides a rich set of additional tools to analyze time resolved data sets of hyperquantitative and gene expression profiles for similarities, including rank correlation, the calculation of regression and correlation coefficients, and clustering. Continuous functions may also be fitted through the data points of individual gene and tissue feature data. Relation between gene expression and hyper-quantitative tissue data may be

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linear or non-linear, in synchronous or asynchronous arrangements.

5 Example 1

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Obesity is increasing at an alarming rate in the United States. In parallel, the incidence of type II diabetes is also rising. We are interested in defining alterations in gene expression that correlate with the development of these conditions in the hopes of reversing these dangerous trends.

Insulin plays a major role in regulating blood glucose levels. It stimulates the uptake of glucose in adipose tissue and striated muscle for storage as intracellular triglycerides and glycogen. Insulin also inhibits the release of glucose from the liver. Normally, this would prevent the rise in blood sugar concentration that occurs after eating. However, in the early stages of type 2 diabetes, resistance to insulin is seen.

Muscle plays a major role in glucose metabolism. Thus, it also is a major contributor to the development of type 2 diabetes. In normal situations, muscle cells respond to increasing levels of insulin by increasing glucose uptake from the bloodstream. However, during the very early stages of type 2 diabetes, muscle tissue becomes resistant to insulin, requiring the pancreatic beta cells to increase insulin secretion. Eventually, the beta cells become unable to compensate for this increasing insulin resistance from muscle and other cells, and insulin production drops. Thus, clinical type 2 diabetes results from the combination of insulin resistance and impaired beta cell function.

Defects in muscle glycogen synthesis are known to play a role in the development of insulin resistance (Petersen and Shulman, 2002). At least three steps - those mediated by glycogen synthase, hexokinase, and GLUT4 - have been reported to be defective in patients with type 2 diabetes. Fatty acids also can induce insulin resistance, and it has been suggested that this was a consequence of altered insulin signaling through PI3-kinase.

We are utilizing a mouse model of diet-induced obesity that progresses to diabetes. The diet is high in fat, an increasing component in the U.S. diet, and has been documented to lead to diabetes in C57BL/6J mice (Surwit et al., 1988). After weaning, C57BL/6J mice were fed either the high fat diet or a standard lab chow diet for 16 weeks. Body weight was monitored bi-weekly. Fasting glucose and insulin levels were measured after 2, 4, 8, and 16 weeks on the diets.

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Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

At each time point, several diabetic and control mice were sacrificed and a number of tissues collected. extracted from the gastrocnemius muscle at each time point.

In order to identify additional muscle genes involved in the development of type 2 diabetes, we used microarray analysis to compare RNA expression levels of 10,000 genes in muscle of high fat diet fed and control diet fed mice at various time points in the progression of type 2 diabetes. Microarray analysis provides a more global picture of gene regulation, allowing the identification of families or groups of genes showing similar expression patterns that potentially imply similar or coordinated roles in disease progression.

Consumption of the HF diet resulted in significant, progressive increases in body weight and fasting insulin levels in comparison to consumption of the Std diet. Fasting glucose levels of mice on the HF diet were dramatically increased at the first time point assayed (2 weeks) and remained high through the duration of the experiment (16 weeks).

Of 10,000 genes analyzed, 121 were up-regulated but only 7 down-regulated greater than two-fold in the diabetic

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relative to non-diabetic mice. These genes are listed in Master Table 1.

This distribution of up- and down-regulated genes was much different from that seen for other organs (liver, pancreas, and white adipose tissue) where there was a much closer balance between the number of up- and down-regulated genes. Actin, alpha, cardiac (Actcl, NM_009608) was one of the most down-regulated genes when comparing HF to Std mice. It was consistently expressed at lower levels in the HF diabetic mice in comparison to the Std mice and also steadily decreased over the 16 week study.

Example 2

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Interestingly, further analysis of the time points and exploration of gene pathways and functionally related genes revealed a subset of actin-related and actin-binding genes exhibiting a consistent decrease in expression (although less than two-fold) in the diabetic mice; 9 of 37 functionally related genes were decreased in diabetic muscle at all four time points and an additional 9 were decreased at three of the four time points. Only two of these genes had been included in the original list of 7 down-regulated genes using the two-fold cut-off criterion.

It is possible that this subtle but coordinated down-regulation of actin-related or actin-binding genes reflects a role in the decreased glucose uptake by skeletal muscle that occurs in diabetes. With nearly half (18 of 37) of the genes in a related family of genes being consistently down-regulated in a study that did not identify a large number of down regulated genes, we feel that actin and genes in actin-related pathways may prove to play key roles in muscle as obesity and diabetes progress.

The actin-related and actin-binding mouse genes in question have been included at the end of Master Table 1, subtable '1A.

Introduction to Master Tables

The master tables reflect applicants' analysis of the gene chip data.

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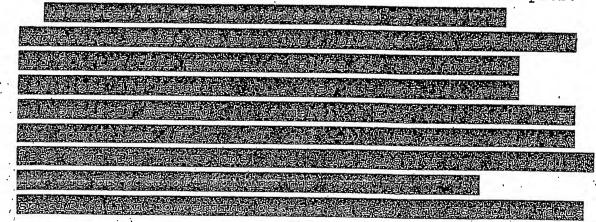
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For each probe corresponding to a differentially expressed mouse gene, Master Table 1 identifies

- Col. 1: The mouse gene (upper) and mouse protein (lower)
 database accession #s.
 - Col. 2: The corresponding mouse Unigene Cluster, as of the $4^{\rm th}$ Quarter 2001 build.
- 15 Col. 3: The behavior (differential expression) observed for the mouse gene. This column identifies the gene as favorable(F) or unfavorable (U) on the basis of its strongest differential behavior at the ages tested. There are three possible comparisons, HI-D, C-HI, and C-D, where C=control (normal), HI=hyperinsulinemic, and D=diabetic. If HI>D, C>HI, or C>D, the behavior for that subject comparison is considered unfavorable. If the inequality is reversed, the behavior for that subject comparison is considered favorable.
 - In the Master Table, the numerical value is the ratio of the greater value to the lesser value. If this ratio is at least two fold, the degree of differential expression is considered strong. Usually only mouse genes exhibiting at least one strong differential expression behavior are listed in the Master Table; exceptions are noted in the Examples.



Col. 4: A related human protein, identified by its database accession number. Usually, several such proteins are identified relative to each mouse gene. These proteins have been identified by BLAST searches, as explained in cols. 6-8.

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Col. 5: The name of the related human protein.

Col. 6: The score (in bits) for the alignment performed by the BLAST program.

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Col. 7: The E-value for the alignment performed by the BLAST program. It is worth noting that Unigene considers a Blastx E Value of less than 1e-6 to be a "match" to the reference sequence of a cluster.

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Unless otherwise indicated, the bit score and E-value for the alignment is with respect to the alignment of the mouse DNA of col. 1 to the human protein of col. 4 by BlastX, according to the default parameters.

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Master Table 1 is divided into three subtables on the basis of the behavior in col. 3. If a gene has at least one significantly favorable behavior, and no significantly unfavorable ones, it is put into Subtable 1A. In the opposite case, it is put into Subtable 1B. If its behavior is mixed, i.e., at least one significantly favorable and at least one significantly unfavorable, it is put into Subtable 1C. Note that this classification is based on the strongest observed differential expression behaviors for each of the three subject comparisons, C-HI, HI-D and C-D.

The corresponding human gene clusters are also of interest. These may be obtained in a number of ways. First, one may

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search on Uniqene

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(http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=unigene) for the identified human protein. Review the "hits" (each of which is a Unigene record) for those prefixed by "Hs." Secondly, one may access the Unigene record for the mouse gene cluster (which is given in Master Table 1), and then click on "Homologene". This will bring up a new page which includes the section "Possible Homologous Genes". One of the entries should be a Homo sapiens gene (considered by Unigene to be the most related human gene); click on its Unigene record link.

Additional information of interest may be accessed by searching with the mouse gene accession # in the Mouse Gene Informatics database, at http://www.informatics.jax.org/.

MASTER TABLE 1 SIGNIFICANTLY DIFFERENTIALLY EXPRESSED MOUSE GENES/ AND CORRESPONDING HUMAN PROTEINS

Subtable 1A: Wholly Favorable Genes and Proteins

17	Behavior Human	Human Protein Name	Score B-value
Proteins			_
F:(IR-D) NP_002408.2 antigon 13.33	2	antigen identified by monoclonal antibody Ki-67; Proliferation-related Ki-67 antigen	. 1711 0
P46013	K167	KI67 HUMAN Antigen KI-67	1711 0
A48666 cell p	cell p	cell proliferation antigen Ki-67, long form	. 1711 0
519.1		antigen of the monoclonal antibody Ki-67	1711 0
!	!	antigen of the monoclonal antibody Ki-67	. 1315 0
B48666 cell p	d [[ec]]	cell proliferation antigen Ki-67, short form	1276 0
F:(IR-D) BAB86352.1 GSK -2.74	1.	GSK-3beta binding protein FRAT1	205 8B-54
AAH34476.1		frequently rearranged in advanced T-cell lymphomas	204 1E-53
		frequently rearranged in advanced T-cell lymphomas	204 2E-53
Q92837 FRT1	FRT	FRT1_HUMAN Proto-oncogene FRAT1 (Frequently rearranged in advanced T-cell	204 2E-53
		lymphomas)	
. AAB97096.2 proto	2	proto-oncogene	204 2E-53
Mm.28479 F:(IR-D) NP_005554.1 stathr -2.54 leuke	.1	stathmin 1; metablastin; prosolin; oncoprotein 18; phosphoprotein 19; stathmin; leukemia-associated phosphoprotein p18	. 286 8B-78
P16949 STN	NIS	STN1_HUMAN Stathmin (Phosphoprotein p19) (pp19) (Oncoprotein 18) (Op18)	286 8E-78
(Leuker protein)	(Leu prote	(Leukemia-associated phosphoprotein p18) (pp17) (Prosolin) (Metablastin) (Pr22 - protein)	
A40936 stathmin	stathr	nin	. 286 8E-78
.1	.1	Pr22 protein	286 8E-78
CAA37391.1 stathmin	.1	nin	· · 286 8E-78
AAA59971.1 oncop	.1	oncoprotein 18	:286 8E-78
AAA59980.1 protein p18	-:	n p18	286 8E-78
CAA64398.1 Pr22	1		286 8E-78
CAC16020.1 dJ12	1	dJ12513.1 (leukemia-associated phosphoprotein p18 (stathmin))	286 8E-78
- AAH14353.1 AAF	1	AAH14353 Similar to stathmin 1/oncoprotein 18	285 2E-77

194 4F-50		194 4E-50	194 4E-50	194 4B-50	170kD); DNA 2463 0			2463 0	2463 0	2462 0	2454 0	2441 0	1923 0	12. 1923 0	II, 180 kD; 1923 0	1923 0	1918 0	1494 0		457 e-128		457 0-128	457 e-128	· 457 e-128	300 3E-81	270 1E-72		g activity (tissue 270 1B-72	
	CAC22254 RB3 protein		12	T_{-}	12			88 TP2A HUMAN DNA topoisomerase II, alpha isozyme	AAC77388.1 topoisomerase II alpha	-					59.2	CAA48197.1 DNA topoisomerase II		AAA61210.1 topoisomerase II	Γ.	NP_076947.1 hypothetical protein MGC2601		CAB56188.1 c380A1.2.1 (novel protein (isoform 1))	AAH00662.1 Unknown (protein for MGC:2601)	AAK61247.1 AE006464 15 unknown	CAB56189.1 c380A1.2.2 (novel protein (isoform 2))	-:		NP 003245.1 itssue inhibitor of metalloproteinase 1 precursor; Erythroid-potentiating activity (tissue	-
,,,,,,,	CACOO	CARG	1 dg	A'AH1				P11388	AAC7	AAA6	CAA0	A40493	002880	A39242	Q AN	CAA	AAC	AAA	<u>.</u>			CAB	AAH	AAK	CAB			0 2	
					F:(IR-D	-2.33		:							<u>.</u>				<u>.</u>		-2.27					F:(TR-D)	-2.18	_	
					Mm.4237	•														Mm.41925					<u>.</u>	Mm.8245	, :.		
					NM 011623	NP_035753.1	•		,											AK007688	AAH37181.1		·			NM_011593	NP_035723.1		

	270 1E-72	.270 1B-72	· 270 1B-72	270 1E-72	270 1E-72	270 1E-72	270 1E-72	270 1E-72	264 8E-71	264 8E-71	236 1E-62	. 221 6E-58	376 e-104	376 e-104	376 e-104	376 e-104	376 e-104	376 e-104	376 e-104	376 e-104	376 e-104	375 e-104	375 e-104 ·	374 e-103	374 e-103 "	373 e-103	372 e-103	371 e-103	371 6-130
(collagenase inhibitor) (Collagenase inhibitor)	metalloproteinase tissue inhibitor 1 precursor [validated]	precursor	prefibroblast collagenase inhibitor	collagenase inhibitor	S68252 1 metalloproteinase inhibitor	AAH00866 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)	erythroid potentiating activity	metalloproteinase inhibitor	B Chain B, Mmp-3TIMP-1 Complex	D Chain D, Mmp-3TIMP-1 Complex	tissue inhibitor of metalloproteinases	AAH07097 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)	thiopurine S-methyltransferase	TPMT HUMAN Thiopurine S-methyltransferase (Thiopurine methyltransferase)	thiopurine methyltransferase	thiopurine methyltransferase; TPMT	thiopurine methyltransferase	thiopurine methyltransferase	thiopurine S-methyltransferase	thiopurine S-methyltransferase	AAH09596 thiopurine S-methyltransferase	thiopurine methyltransferase	thiopurine methyltransferase	thiopurine S-methyltransferase	thiopurine methyltransferase	thiopurine methyltransferase	AAH05339 thiopurme S-methyltransferase	thiopurine methyltransferase	Highinina S-methyltraneferses
·	ZYHUEP	CAA26902.1	AAA52436.1	A;AA63234.1	A:AD14009.1	AAH00866.1	1107278A	1308125A	1UEA	1UEA	BAA01913.1	AAH07097.1	NP_000358.1	P51580 ··	157946	AAB27277.1	AAC50130.1.	A:AC50368.1	AAC51865.1	BAA97037.1	A:AH:09596.1	AAB71630.1	AAB71626.1	AAB80746.1	AAB71629.1	A'AB71627.1	AAH05339.1	AAB71625.1	A A B 807/7 1
							,	•					Mm.10169 F:(IR-D) -2.18		•								• •						
										·			NM_016785 NP_058065.1		,														

			AAC50129.1	thiopurine methyltransferase	26	265 9E-84	7.
				similar to thiopurine methyltransferase	265	5 6E-83	33
U08020 AAA88912.1	Mm.22621 F:(IR-D)		P02452	CA11_HUMAN Collagen alpha 1(I) chain precursor	48	486 e-136	و
			AAB94054.2	pro alpha 1(1) collagen	· 48	486 e-136	9
			NP_000079.1	alpha 1 type I collagen preproprotein; Collagen I, alpha-1 polypeptide; osteogenesis imperfecta type IV; collagen of skin, tendon and bone, alpha-1 chain	48	484 e-136	. : و
			CAA98968.1	prepro-alpha1(I) collagen	4	484 e-136	9
	-		CGHUIS	collagen alpha 1(T) chain precursor	4		و
			AAA51995.1	alpha 1 (I) chain propeptide	48	482 e-135	55
			AAH36531.1	Unknown (protein for MGC:33668)	4	480 e-135	.5
			AAB27856.1	type I collagen pro alpha 1(I) chain propeptide	4(469 e-131	11
			CAA29605.1	C-terminal propeptide domain	4	435 e-121	[[
	•		CAA29604.1	pro-alpha 1 (II) collagen (313 AA; AA 975-271c)	3,	372 0-102	. 2
			NP_001835.2	alpha 1 type II collagen isoform 1; collagen II, alpha-1 polypeptide; cartilage collagen; chondrocalcin, included; COL11A3, formerly	 	372 e-102	
			AAC41772.1	alpha-1 type II collagen	. 3,	372 e-102	.2
					Ī	:	
NM_023043 NP_075530.1	Mm.18075 F:(IR-D) 0 -2.14	F:(RR-D) -2.14	NP_036541.1	prion gene complex, downstream	. 2	283 1E-75	75
-			Q9UKY0	PRND HUMAN Prion-like protein doppel precursor (PrPLP) (Prion protein 2)	2	283 1E-75	75
			AAF02424.1	AF106918 1 prion-like protein	2	283 1E-75	75
			CAB75502.1	dJ1068H6.4 (prion protein like protein doppel)	7.	282 2E-75	75
•			AAG43449.1	prion-like protein	2	281 3E-75	75
			AAG43448.1	AF187843 1 doppel protein	7.	246 2E-64	64
NM_009464	Mm.6254	Ą	NP_003347.1	uncoupling protein 3, isoform UCP3L	5	531 e-151	51.
NP 033490.1		/0.~-	•			· · ·	•
	·	:	P55916	UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)	5	531 e-151	51 .
			JC5522	uncoupling protein UCP3, mitochondrial	<u> </u>	531 e-151·	51.
			AAC51367.1	UCP3	. 5	531 e-151	21
	·		AAC51369.1	uncoupling protein 3	5	531 e-151"	E

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e-151	e-151	e-149	e-144	464 e-131	464 e-131	e-129	456 e-128.	456 e-128	·· ·	e-128	e-128	456 e-128	e-128	e-128	e-128	7E-95	7E-95	7E-95	- 46-39	342 6E-94	2E-55	309 9E-84		2E-76	2E-76	•
531	531	525	510	464	464	457	456	456		. 456	456	456	456	456	456	. 345	345	345	342	342	214	309		285	285	٠
uncoupling protein-3	AF050113_1 uncoupling protein-3	uncoupling protein 3	uncoupling protein 3	uncoupling protein 3, isoform UCP3S	UCP3S	uncoupling protein-2	uncoupling protein 2	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP. 2) (UCPH)		UCP2	uncoupling protein 2	uncoupling protein-2	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)	uncoupling protein homolog	uncoupling protein 2	uncoupling protein 1; mitochondrial brown fat uncoupling protein	uncoupling protein 1, mitochondrial	uncoupling protein	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	uncoupling protein				potassium channel, subfamily K, member 16; pancreatic 2P domain potassium channel TAIK.1	CIWG HUMAN Potassium channel subfamily K member 16 (TWIK-related alkaline	pri activated K+ channel 1) (2P domain potassium channel Talk-1)
AAC51767.1	AAG02284.1	AAC18822.1	AAC51785.1	NP 073714.1	AAC51356.1	AAB48411.1	NP_003346.2	P55851		AAC51336.1	AAC39690.1	AAD21151.1	AAH11737.1	AAB53091.1	CAA11402.1	NP 068605.1	G01858	A'AA85271.1	P25874	CAA36214.1	AAH08392.1) CAC07336.1		NP_115491.	Q96T55	
	·																		· ·		·	F:(IR-D -2.06				
			:					. :				·										Mm.10557 F:(IR-D) 1				
						i				•	·	·										AK014626	XP 138942.1			

255 SE-67		255 5E-67	255 SB-67	255 SE-67	255 SB-67	5E-67	SE-67	5E-67	255 SE-67	255 SE-67	255 SE-67	SE-67	255 5E-67	255 5E-67	255 5E-67	254 1E-66	250 2E-65	2E-65	249 3E-65	249 3B-65	223 2E-57	448 e-125	446 e-125	446 e-125	446 e-125	446 e-125	e-125 ·	446 e-125	446 e-125
255	:	255	255	255	255	255	. 255	255	. 255	.255	. 255	255	255	255	. 255	254	250	250	249	249	223	. 448	446	446	446	446	446	446	446
Mm.3862 F:(RD) NP_000603.1 insulin-like growth factor 2 (somatomedin A); somatomedin A		IGF2_HUMAN Insulin-like growth factor II precursor (IGF-II) (Somatomedin A)	nsulin-like growth factor II precursor [validated]	IGF-II precursor	precursor polypeptide (AA -24 to 156)	preproinsulin-like growth factor II, domains A-E	insulin-like growth factor	insulin-like growth factor II precursor	insulin-like growth factor II	insulin-like growth factor II; IGR-II	AF217977 1 unknown	AAH00531 insulin-like growth factor 2 (somatomedin A)	AF517226 1 insulin-like growth factor 2 (somatomedin A)	insulin-like growth factor II precursor	insulin-like growth factor II	insulin-like growth factor II precursor	insulin-like growth factor II, domains A-B	preproinsulin-like growth factor II, domains A-E	insulin-like growth factor II precursor, splice form II	put. IGF-II	precursor polypeptide (AA -24 to 140)	AAH07725 ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive with mental retardation)	ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive with mental retardation)	CLN8 HUMAN CLN8 protein	AF123757 1 putative transmembrane protein	AF123758 1 putative transmembrane protein	AF123759 1 putative transmembrane protein	AF123760 1 putative transmembrane protein	AP123761 1 putative transmembrane protein
NP_000603.1	· ·	P01344	IGHU2	CAA25426.1	CAA29516.1	AAA52442.1	AAA52535.1	AAA52545.1	AAA60088.1	AAB34155.1	AAG17220.1	AAH00531.1	AAM51825.1	1009249A	1203258B	AAA52544.1	167610	A:AA52443.1	S02423	CAA27249.1	CAA29517.1	AAH07725.1	NP 061764.1	Q9UBY8	AAF13115.1	AAF13116.1	AAF13117.1	AAF13118.1	AAF13119.1
F:(TR-D)	0 0 7							·		i												F:(IR-D) -2.09							
Mm.3862	•																					Mm.21578	,						
NM_010514						,			٠					÷					٠			NM_012000 NP_036130.1	,						

E-94	2E-94	E-93	E-93	E-93	1E-93	1E-65	1E-65	E-65	E-65	249 1E-65	248 2E-65	245 2B-65	217 SE-56	217 SE-56	5E-56	7E-53·	7B-53	0	:				. 0	e-143·	e-140	e-140	499 e-140
345 2E-94	345 2	342 1E-93	342 1E-93	- 342 1E-93	342 1	249 1	249 1	249 1E-65	249 IE-65	249 1	248	245	217	217	217	206 7	206 7E-53	. 808	<u>-</u>	0 208	807	· ·.	807	. 507	499	664 .	499
similar to data source:MGD, source key:MGI:98241, evidence:ISS~putative~superiorcervical ganglia, neural specific 10	AAH06302 Similar to superiorcervical ganglia, neural specific 10		П	STN2_HUMAN Stathmin 2 (SCG10 protein) (Superior cervical ganglion-10 protein)	silencer element	2 SCG10-like-protein		SCG10 like-protein	bK3184A7.2 (SCG10-like protein (SCLIP) (ortholog of rabbit neuroplasticin-2 (NPC2)))	AAH09381 Unknown (protein for MGC:16668)		unnamed protein product	STN4 HUMAN Stathmin 4 (Stathmin-like protein B3) (RB3)	RB3 protein	hypothetical protein	2 stathmin-like-protein RB3				1 nuclear factor I/B		(CCACA1-50x omaing transcription factor) (LLF) (LGGCA-5inoing protein)	1 nuclear factor I-B2	1. Inuclear factor 1 B-type	1 nuclear factor I/C (CCAAT-binding transcription factor)		
XP_170521.1	AAH06302.1	NP_008960.1	AAB36428.1	Q93045	BAA23326.1	NP 056978.2	Q9NZ72	AAF35245.1	CAC16222.1	AAH09381.1	AAD12730.1	BAC11252.1	Q9H169	CAC22254.1	CAB66503.1	NP 110422.	AAH11520.1	AAH01283.1		MP 005587.	000712	•	AAB41899.1	AAA93125.1	NP 005588.	CAA63440.1	AAH12120.1
F:(C-IR) 4.72									,	٠								F:(C-IR)	-2.69			•					
Mm.29580 F:(C-IR) -4.72													•	:				Mm.4025			2	•		:			
NM_025285 NP_079561.1			٠															NM_008687	NP 032713.1								

137	· ·	e-136	136 .	e-136			136	e-136	2E-91	4E-89	4E-89	3-86	B-76	92 - 2	0-111 -	·•		%. !!!	111	111	e-111	111	_	101	 .	e-101	e-101	e-101	.101	.101
487 e-137	•	484 e-]	484 e-136	483 e-1	· .	1	483 e-136	483 e-	334 2E	326 4E	326 4E	317 2E-86	284 2E-76	284 2E-76	402 e-	· :	100	402 c-	. 402 e-111	402 e-111	402 e-	402 e-111		365 e-101	•	365 e-	365 e-	365 e-	365 e-101	.365 e-101
NFIC_HUMAN Nuclear factor 1 C-type (Nuclear factor 1/C) (NF1-C) (NFI-C) (NF-I/C)	(Control duming tunned poor (Control of Control of Cont	nuclear factor I	KIAA1439 protein	NFIA_HUMAN Nuclear factor 1 A-type (Nuclear factor 1/A) (NF1-A) (NFI-A) (NF-	[I/A] (CCAAT-box binding transcription factor) (CTF) (TGGCA-binding protein)		7 similar to transcription factor NF1	Nuclear Factor IA	SELT_HUMAN Selenoprotein T	1 selenoprotein T	selenoprotein T	similar to Selenoprotein T	Unknown	Unknown (protein for MGC:45090)	1 TERA protein		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	nypothetical protein DKFZp/6ZL137.1	hypothetical protein	AF212220 1 TERA	unnamed protein product	AAH00024 TERA protein		TPM3_HUMAN Tropomyosin alpha 3 chain (Tropomyosin 3) (Tropomyosin gamma)		5 similar to tropomyosin, fibroblast	tropomyosin NM, skeletal muscle	skeletal muscle tropomyosin (AA 1-285)	1 AAH08407 Unknown (protein for MGC:14532)	1 AAH08425 Unknown (protein for MGC:14582)
P08651		B33416	BAA92677.1	Q12857	. :		XP 046827.7	AAH22264.1	EIZN6D	NP 057359.1	A'AF13696.1	XP 088553.	A:AD20063.1	AAH36738.1	NP_067061.1		TACO10	140918	CAB75656.1	AAF87322.1	BAB15592.1	AAH00024.1		P06753		XP 036829.5	A24199	CAA27798.1	AAH08407.1	AAH08425.1
	•			:					Mm.28026 F:(C-IR)						Mm.18637 F:(C-IR)	-2.4		•						(R)	-4.34					
	,			÷	:				AK013022 Q9NZJ3					•		NP_062617.1				;				NM_022314	1.60/1/0-1v1					

-101	3E-95	345 8E-95	3E-95	326 3E-89	326 3E-89	326 3E-89	325 7E-89	315.9E-86	315 9E-86	310 2E-84	300 2E-81	1E-75	1E-75	1E-75	1E-74	1E-74	308 SE-83	·.·	5E-83	543 e-154.		e-154	e-154	e-154	e-154	e-154	e-154	e-154 .	541 e-154
365 e-101	. 345 8E-95	345	345 8E-95	326	:326	326	325 7	315.9	315	310	300	281	281	281	. 278	278	308		308	543		543	543	543	543	543	543	543	541
						•	· .			 :								i .		·		·	:						
				pomyosin)																									
tropomyosin	TPM1 HUMAN Tropomyosin 1 alpha chain (Alpha-tropomyosin)	tropomyosin alpha chain, cardiac and skeletal muscle	skeletal muscle tropomyosin	TPM2 HUMAN Tropomyosin beta chain (Tropomyosin 2) (Beta-tropomyosin)	tropomyosin beta, skeletal muscle	beta-tropomyosin (AA 1-284)	AAH07433 Similar to tropomyosin 1 (alpha)	tropomyosin 3	unnamed protein product	skeletal muscle tropomyosin	unnamed protein product	tropomyosin 1 (alpha)	tropomyosin 3, fibroblast	tropomyosin	tropomyosin	hypothetical protein	hypothetical protein FLJ21195 similar to protein related to DAC		unnamed protein product	cyclin G1		1_HUMAN Cyclin G1 (Cyclin G)	cyclin G1	cyclin G1	cyclin G1		cyclin G1	cyclin G1	cyclin G1
top	TPIN	tropo	skele	TPN	trop	beta	AAF	trop	nung	skel	euun	trop	frop	trop	trop	hype	hypc		nany	cycl		CGG1	cycl	cycl	cycl	cyclin G	cycl	cycl	cycl
1209280A	P09493	A25825	AAA61225.1	P07951	S00922	CAA29971.1	AAH07433.1	NP 689476.1	BAC03946.1	AAA61226.1	BAB14554.1	NP 000357.2	A'27674	AAA36771.1	T08796	CAB43309.1	NP_071914.1		BAB15026.1	NP_004051.1		P51959	G02401	AAC41977.1	ÀAC50688.1	BAA11353.1	AAH00196.1	2210321A	AAH07093.
:													:							F:(C-IR)	7.7-								
		,			·		•	Ĭ	i						:		Mm.25760 F:(C-IR)			Mm.2103									
				;			·			·					•		NM_011825 NP_035955.1		·	NM_009831	NP 033961.1	:			·				

			Г		514	514 P-146
	1			cycim G	717	1250
			CAA54821.1	cyclin G1	407	e-130
				cyclin G	421	e-117
			AAB03903.1	cyclin G	421	421 e-117
				Similar to cyclin G2	292	292 8E-79
			-	cyclin G2	. 292	8E-79
			Q16589	CGG2_HUMAN Cyclin G2	292	292 8E-79
			AAC41978.1	cyclin G2	292	8E-79·
			AAC50689.1	cyclin G2	292	8E-79
•			A:AN40704.1	cyclin G2	292	8E-79
		·	2210321B -	cyclin G2	.292	6 <i>L-</i> ∃8
	Mm.21758 F:(C-IR)	F:(C-IR)	NP_000764.1	cytochrome P450, subfamily IIB, polypeptide 1; microsomal monooxygenase;	792	0
NP_067257.1		-2.19 F.(C-D) - 2.5		xenobiotic monooxygenase; flavoprotein-linked monooxygenase; cytochrome P450, subfamily IIB (ethanol-inducible)		, * <u>*</u>
			P05181	CPB1 HUMAN Cytochrome P450 2B1 (CYPHB1) (P450-J)	792	0
			A31949	cytochrome P450 2E	792 0	0
			AAA52155.1	cytochrome P450IIE1	792	. 0
100		,	AAA35743.1	cytochrome P450j	792	. 0
		·	AAF13601.1	AF182276 1 cytochrome P450-2B1	. 790	0
			AAD13753.1	cytochrome P450 2B1	751	0
			NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19;	. 557	e-158
	; '	· ·		mephenytom 4-nydroxylase; mcrosomal monooxygenase; xenopione monooxygenase; flavoprotein-linked monooxygenase		•
	١.		P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYPIIC19) (P450-11A) (Mephenytoin 4-hydroxylase) (CYPIIC17) (P450-254C)	557	e-158
			AAB59426.1	cytochrome	557	e-158
	·		NP_000763.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18;	955	e-158
• • • • • • • • • • • • • • • • • • • •		•		cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 17; microsomal monooxygenase; flavoprotein-linked monooxygenase	;···	•
•			AAB59356.1	cytochrome	955 .	e-158
	٠		P33260	CPCI_HUMAN Cytochrome P450 2C18 (CYPIIC18) (P450-6B/29C)	553	e-157
	:- :		A61269	cytochrome P450 2C18	553	e-157
			AAA02630.1	cytochrome P-4502C18	. 553	e-157

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550 e-156	e-156.	e-156.	550 e-156	550 e-156	e-156	e-155	9E-69		258 9E-69	258 9E-69.	9E-69	4E-68	o [.] .	· ·	0	0	. 0	0		0	0	0.
550	550	.550	550	. 550	550	545	. 258	;; ;	258	258	. 258	~ 256	2244		2244	2244 0	2244 0	1628	· ·	1628	1628	1628
cytochrome P-450	T	CPC9_HUMAN Cytochrome P450 2C9 (CYPIIC9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)	S-mephenytoin 4-hydroxylase (BC 1.14.14) cytochrome P450 2C9	cytochrome P450	S-mephenytoin 4'-hydroxylase (BC 1.14.14) cytochrome P450 2C19	Ι.			polymerase (RNA) III (DNA directed) polypeptide K (12.3 kDa)	hypothetical protein FLJ22940	AE006462 3 Minus -99 protein		1 phosphorylase kinase, alpha 1 (muscle); phosphorylase kinase, alpha 1 (muscle), muscle glycogenosis; Phosphorylase kinase, muscle, alpha polypeptide		KPB1_HUMAN Phosphorylase B kinase alpha regulatory chain, skeletal muscle: isoform (Phosphorylase kinase alpha M subunit)	phosphorylase kinase (EC 2.7.1.38) alpha-1 chain	l phosphorylase kinase	1 phosphorylase kinase, alpha 2 (liver); Phosphorylase kinase deficiency, liver (glycogen storage disease; phosphorylase kinase, alpha 2 (liver), glycogen storage disease IX		KPB2_HUMAN Phosphorylase B kinase alpha regulatory chain, liver isoform (Phosphorylase kinase alpha L subunit)	1 phosphorylase kinase	1 phosphorylase kinase alpha subunit
BAA00123.1	NP_000762.2	P11712	B38462	1313295A	F38462	AAB23864.2	NP_078847.1		AAH01381.1	AAH09179.1	AAK61211.1	BAB15505.1	NP_002628.1	,	P46020	138111	CAA52083.1	NP_000283.1	:. :	P46019	CAA56662.1	BAA07606.1
							F:(C-IR)	-2.19	:				F:(C-IR) -2.18	•			:	,				
							Mm.29952 F:(C-IR)	+1		:			Mm.42254 F:(C-IR)					• • •				
					·		AK019452	BAB31728.1					NM_008832	NP_032858.1			i		•	;		

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1628 0	. 1624 0.	631 e-180	473 e-132	· · - · · 461 e-129	. 461 e-129	465 e-131	•	465 e-131	465 e-131	465 e-131	. 465 e-131	465 e-131	465 e-131	343 2E-94		- 343 2B-94	· 343 2E-94	341 1E-93	. 341 1E-93	341 1E-93	340 2E-93	340 2E-93	340 2E-93	340 2E-93	cin 328 9E-90		ein 328 9E-90		
phosphorylase kinase alpha subunit	AAH14036 Similar to phosphorylase kinase, alpha 2 (liver)	d1499B10.2 (phosphorylase kinase, alpha 2 (liver) (PYK))	phosphorylase kinase alpha subunit liver isoform, PHKA2 {BC 2.7.1.38} [human, hepatoma, Peptide Partial, 377 aa]	phosphorylase kinase (EC 2.7.1.38) beta chain	Similar to phosphorylase kinase, beta	hypothetical protein		hypothetical protein	AAH11647 Similar to hypothetical protein	AAH12802 Similar to hypothetical protein	hypothetical protein	hypothetical protein FLJ21827	unnamed protein product	retinol-binding protein 4, plasma precursor		plasma retinol-binding protein precursor	precursor RBP	Plasma retinol-binding protein precursor (PRBP) (RBP) (PRO2222)	Similar to retinol binding protein 4, plasma		Retinol Binding Protein	Retinol Binding Protein (Holo Form)	Retinol Binding Protein (Apo Form)	retinol binding protein	E.Chain B, The Structure Of Human Retinol Binding Protein With Its Carrier Protein	Transthyretin Reveals Interaction With The Carboxy Terminus Of Rbp	F Chain F, The Structure Of Human Retinol Binding Protein With Its Carrier Protein Transferration Desirals Internation With	The Carboxy Terminus Of Rbp	•
AAD32846.1	AAH14036.1	CAB86408.1	AAB27307.1	S74251	AAH33657.1	CAB96537.1		CAB66868.1	AAH11647.1	A:AH12802.1	AAH22856.1	NP 064538.2	BAB15146.1	NP_006735.1		pir VAHU	CAA24959.1	P02753	AAH20633.1	XP 005907.5	IRBP	1BRP	1BRQ -	1401251A	1QAB		1QAB	•	
					-	F:(C-R)	-2.16							F:(C-IR)	-2.15														
		•				Mm.30006 F:(C-IR)	·.			,			-	Mm.2605											•	·	· :		
					·	\top	NP_076320.1				÷			AK004839	XP 129259.1													.,	

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	7(CDC37))				60	00		60	60	60		<u> </u>
	rotein 37(CDC37))	rotein 37(CDC37))	rotein 37(CDC37))	rotein 37(CDC37)) 639 omolog); CDC37 (S	rotein 37(CDC37)) comolog); CDC37 (S	rotein 37(CDC37)) omolog); CDC37 (S	rotein 37(CDC37)) comolog); CDC37 (S protein kinase-targeti	rotein 37(CDC37)) comolog); CDC37 (S. protein kinase-targeti	rotein 37(CDC37)) comolog); CDC37 (S protein kinase-targeti protein kinase-targeti	rotein 37(CDC37)) comolog); CDC37 (S protein kinase-targeti g)	rotein 37(CDC37)) comolog); CDC37 (S. protein kinase-targeti ng)	rotein 37(CDC37)) comolog); CDC37 (S. protein kinase-targeti ng)
GPR34	GPR34	: GPR34 cle control protein 3 otein FLJ20639	: GPR34 cle control protein 3 otein FLJ20639	GPR34 cle control protein 2 otein FLJ20639 cerevisiae, homolog	GPR34 cle control protein 2 otein FLJ20639 cerevisiae, homolog	GPR34 cle control protein 2 cerevisiae, homolog chaperone protein	GPR34 cle control protein 2 otein FLJ20639 cerevisiae, homolog chaperone protein	c GPR34 cle control protein 3 otein FLJ20639 cerevisiae, homolog chaperone protein siae, homolog)	GPR34 cle control protein 2 cerevisiae, homolog chaperone protein chaperone protein siae, homolog)	cerevisiae, homolog chaperone protein siae, homolog)	cle control protein 3 cerevisiae, homolog chaperone protein siae, homolog) siae, homolog)	cerevisiae, homolog care, homolog siae, homolog)
GP34 HUMAN Probable G protein-coupled receptor GPR34 orphan G protein-coupled receptor unnamed protein product AAH20678 G protein-coupled receptor 34	pled receptor GPR 34 Il division cycle co	pled receptor GPR 34 Il division cycle co 2.20783) pothetical protein	pled receptor GPR 34 Il division cycle co 2:20783) pothetical protein]	pled receptor GPR 34 Il division cycle corpothetical protein pothetical protein cycle 37, S. cerevi	pled receptor GPR 34 1 division cycle coi 20783) pothetical protein] cycle 37, S. cerevi dc37 (Hsp90 chap	pled receptor GPR 34 1 division cycle co pothetical protein J cycle 37, S. cerevi dc37 (Hsp90 chap	pled receptor GPR 34 1 division cycle coi pothetical protein] cycle 37, S. cerevi dc37 (Hsp90 chap	pled receptor GPR 34 1 division cycle coi pothetical protein] cycle 37, S. cerevi dc37 (Hsp90 chap.	pled receptor GPR 34 1 division cycle coi pothetical protein J cycle 37, S. cerevi 37, S. cerevisiae, 1 37, S. cerevisiae, 1 37, S. cerevisiae, 1	pled receptor GPR 34 1 division cycle col pothetical protein J cycle 37, S. cerevi 37, S. cerevisiae, I 37, S. cerevisiae, I 37, S. cerevisiae, I	pled receptor GPR 34 !:20783) pothetical protein J cycle 37, S. cerevi 37, S. cerevisiae, I 37, S. cerevisiae, I anscription factor	1 division cycle collothetical protein J pothetical protein J pothetical protein J cycle 37, S. cerevisiae, 1 37, S. cerevisiae, 1 37, S. cerevisiae, 1 37, S. cerevisiae, 1 chascription factor
ceptor ed receptor 34	ceptor ed receptor 34 similar to cell div	ceptor ed receptor 34 similar to cell div ein for MGC:207	ceptor ed receptor 34 similar to cell div ein for MGC:207 of Cdc37; hypoth	ceptor ed receptor 34 similar to cell div of Cdc37; hypoth cell division cycl	ceptor ed receptor 34 similar to cell division cycl cell division cycl chaperone Cdc3	ed receptor 34 similar to cell diversion cycle division cycle chaperone Cdc3*	ed receptor 34 similar to cell div f Cdc37; hypoth cell division cycl chaperone Cdc3	ed receptor 34 similar to cell division cycle 37, vision cycle 37,	ed receptor 34 similar to cell diversion cycle 37, vision	ed receptor 34 ed receptor 34 similar to cell div of Cdc37; hypoth cell division cycle 37, vision cycle 37,	ed receptor 34 ed receptor 34 ein for MGC:207 of Cdc37; hypoth cell division cycle chaperone Cdc37 vision cycle 37, vision cycle 37, rision cycle 37, rision cycle 37, rision cycle 37,	ed receptor 34 ed receptor 34 similar to cell division for MGC:20 of Cdc37; hypoth cell division cycle 37, vision cycle 37, vision cycle 37, vision cycle 37, vision cycle 37, zinc finger transe
orphan G protein-coupled receptor unnamed protein product AAH20678 G protein-coupled receptor 34	in product protein-coupled protein-coupled covel protein sim	in product protein-coupled protein-coupled lovel protein sim nknown (protein ting relative of C	in product protein-coupled protein-coupled lovel protein sim nknown (protein ting relative of (in product protein-coupled protein-coupled tovel protein sim nknown (protein ting relative of (zin product zin product log; CDC37 (cel molog	in product protein-coupled protein-coupled lovel protein sim ling relative of (zin product ling roduct log; CDC37 (cel log; CDC37 (cel molog N Hsp90 co-chz dc37)	in product protein-coupled protein-coupled wel protein sim denown (protein ting relative of C in product log; CDC37 (cel molog N Hsp90 co-chi Zdc37) log	in product protein-coupled protein-coupled ovel protein sim ovel protein sim drnown (protein ting relative of (2 in product sin product log; CDC37 (cel molog N Hsp90 co-chz AN Hsp90 co-chz dc37)	in product protein-coupled protein-coupled protein-coupled lovel protein sim ling relative of (in product ling product log; CDC37 (cel molog N Hsp90 co-chz Oc37) log	in product protein-coupled in protein-coupled ovel protein sim ovel protein sim drnown (protein ting relative of (sin product sin product og; CDC37 (cel molog N Hsp90 co-chz Zdc37) og og og DC37 (cell divis DC37 (cell divis DC37 (cell divis)	in product protein-coupled in product lovel protein sim ling relative of (sin product sin product log; CDC37 (cel molog N Hsp90 co-chz Jdc37) log Log Log Log Log Log Log Log	in product protein-coupled protein-coupled lovel protein sim lovel protein sim ling relative of (log; CDC37 (cel molog IN Hsp90 co-chz 2dc37) log	in product protein-coupled protein-coupled lovel protein sim ling relative of (sin product sin product log; CDC37 (cel molog N Hsp90 co-chz dc37) log log log log DC37 (cell divis DC37 (cell divis log log Struppel-like fac Kruppel-like zin actor
umamed protein product AAH20678 G protein-co	AAH20678 G pr AAH20478 G pr AA6724.4 (A nov	AAH20678 G pr AAH204.4 (A nov AAH14133 Unks Hsp90-associatir	AAH20678 G proAAH20678 G proA6124.4 (A nov AAH14133 Unko Hsp90-associatirumamed protein	AAH20678 G property of the pro	AAH20678 G pro-AAH14133 Unko HSp90-associatir umnamed protein CDC37 homolog ccrevisiae) homo CC37_HUMAN subumit) (p50Cd	AAH20678 G property of the pro	AAH20678 G property of the pro	AAH20678 G property of the pro	AAH20678 G property of the pro	AAH20678 G proper and a protein and a protei	AAH20678 G probable of property of the propert	AAH20678 G property of the pro
AAH20678.1 A					78.1 :	78.1 05.1 33.1 383.1 04.1 06.1	78.1 05.1 06.1 06.1 996.1	78.1	78.1 05.1 06.1 06.1 996.1 779.1 98.1 98.1	78.1	78.1 05.1 06.1 133.1 104.1 106.1 106.1 1079.1 108.	78.1 :
AA												
	8875 F:((8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C	8875 F:(C
	Mm.78	Mm.78	Mm.78	Mm.78	Mm 78	Mm.78	Мт.78	Mm.78	Мт.78	Mm 78	Mm. 29	Mm 78
		NM_025950_N NP_080226.1										
	Mm.78875 F:(C-IR) CAC12705.1 -2.08	Mm.78875 F:(C-IR) CAC12705.1 -2.08 	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91206.1	Mm.78875 F:(C-IR) CAC12705.1 -2.08	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91206.1 NP_008996.1	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91206.1 NP_008996.1 O16543	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91304.1 BAA91306.1 NP_008996.1 Q16543 Q16543	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91206.1 NP_008996.1 Q16543 Q16543 AAB63979.1 AAB63979.1 AAB64798.1	Mm.78875 F:(C-IR) CAC12705.1 -2.08 -	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91304.1 BAA91306.1 C16543 C16543 C16543 C16543 AAB04798.1 AAH00083.1 Mm.26938 F:(C-IR) AAD55891.1	Mm.78875 F:(C-IR) CAC12705.1 -2.08 -2.08 AAH14133.1 NP 060383.1 BAA91304.1 BAA91304.1 BAA91304.1 BAA91304.1 BAA91304.1 BAA91304.1 AAB63979.1	Mm.78875 F:(C-IR) CAC12705.1 -2.08 AAH14133.1

			, 25, 100	CARL	21	213 5B-55
			62.1		1	22.77
:	-		043474	KLF4_HUMAN Kruppel-like factor 4 (Epithelial zinc-finger protein EZF) (Gut-	. ż	, č-4c si ž
			╗	enriched Krueppel-like factor)	j	1
			AAD42165.1	AF105036 1 zinc finger transcription factor GKLF	213	3 5E-55
				Kruppel-like factor 4 (gut)	213	
		•	-	Kruppel-like factor 4 (gut); endothelial Kruppel-like zinc finger protein	. 213	3 SE-55
		•:	AAB48399.1	NEZH.	213	3 5E-55
		٠.	AAH30811.1	Similar to Kruppel-like factor 4 (gut)	213	
			AAH35342.1	Similar to Kruppel-like factor 2 (lung)	211	1 3E-54
NM_020007	Mm.14199 F:(C-IR)	F:(C-IR)	AAK94915.1	AF401998_1 muscleblind 41kD isoform	<u> 5</u> 69	9 e-166
NP_064391.1	: :	-2.04				
			NP 066368.1	muscleblind (Drosophila)-like	546	6 e-160
			BAA24858.1	KIAA0428	. 57	546 e-160
			09NR56	MBNL HUMAN Muscleblind-like protein (Triplet-expansion RNA-binding protein)		537 e-157
•						
·			CAA74155.1	MBNL protein	.5.	537 e-157
			NP 659002.1	muscleblind-like protein MBLL39 isoform 1	4	449 e-125
	·		AAM09798.1	AF491866 1 muscleblind-like protein MLP1	4	449 e-125
		: ::.	AAM50085.1	muscleblind-like protein MBLL39	. 4.	427 e-119
			NP 060858.2	CHCR isoform G	. 3	387 e-106
	٠.		Q9NUK0	MBXL_HUMAN Muscleblind-like X-linked protein (Cys3His CCG1-required protein) (HCHCR protein)	. 3	387 e-106
			AAL65661.1	CHCR isoform G	3	387 e-106
		:	BAB85648.1	hCHCR-G	-3	387 e-106
			CAD20869.1	CHCR protein	3	387 e-106
			AAM09533.1	AF491305 1 MBLX39	3	387 e-106
			NP 005748.1	muscleblind-like protein MBLL39 isoform 2	3.	377 e-103
			AAC67242.1	zinc finger protein	3	377 e-103
			BAB85649.1	hCHCR-R	3	343 1E-93
·		·	CAD20870.1	CHCR protein	3	343 1E-93
			AAL87670.1	AF467070 1 Cys3His CCG1-required protein isoform R	3	343 1E-93
			AAK82889.1	AF395876 1 36 kDa muscleblind protein BXP36	. 2	286 TE-82
NM 009883	Mm.4863	F:(C-IR)	CAC14276.1	bA112L6.1 (CCAAT/enhancer binding protein (C/BBP), beta)	2	271 2E-72

NP 034013.1		-2.03				
			AAH07538.1	Unknown (protein for MGC:15409)	. 271	2E-72
·			AAL55792.1	AF289608_1 unknown	271	2E-72
3			AAH21931.1	Unknown (protein for MGC:32080)	. 271	2E-72
	·	•	AAN86350.1	CCAAT/enhancer binding protein (C/EBP), beta	271	2E-72
			NP_005185.1	CCAAT/enhancer binding protein (C/EBP), beta; CCAAT/enhancer-binding protein	271	2E-72
	,		•	(C/EBP), beta (transcription factor-5)		
**	•		P17676	CEBB_HUMAN CCAAT/enhancer binding protein beta (C/EBP beta) (Nuclear factor	271	2E-72
				NF-IL6) (Transcription factor 5)		
	·		S12788	transcription factor NF-IL6	. 271	2E-72
		·	CAA36794.1	nuclear factor NF-IL6 (AA 1-345)	. 27	271 2E-72
AK004002	Mm.19844 F:(C-IR)	F:(C-IR)	CAA36441.1	five-lipoxygenase activating protein (FLAP)	. 28	282 4B-76
BAB23117.1	· .	-2.02			•	: .
			NP_001620.2	arachidonate 5-lipoxygenase-activating protein; five-lipoxygenase activating protein; MK-886-binding protein	282	4B-76
	·		P20292	FLAP_HUMAN 5-lipoxygenase activating protein (FLAP) (MK-886-binding protein)	282	2 4E-76
	:		A39824	5-lipoxygenase-activating protein	282	2 4E-76
:			AAA35845.1	5-lipoxygenase activating protein	282	2 4E-76
			1603359A	lipoxygenase activating protein	.27	279 3E-75
NM_009776	Mm.38888 F:(C.IR)	F:(C-IR)	AAH11171.1	serine (or cysteine) proteinase inhibitor, clade G (Cl inhibitor),member 1	, 199.	634 0
NP 033906.1	,	-2.02				
			P05155	IC1_HUMAN Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh)	633	0
,			ITHUC1	complement C1 inhibitor precursor [validated	633	0
٠		,	CAA38358.1	C1 inhibitor	.63	633 0
-			CAA30314.1	C1 inhibitor	633	30
			AAM21515.1	AF435921_1 C1 esterase inhibitor	~ 633	0
			NP_000053.1	complement component 1 inhibitor precursor; serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor), member 1	. 63,	632 0
			AAB59387.1	plasma protease (CI) inhibitor precursor	. 63,	632 0

· .		:	P58340 	MLF1_HUMAN Myeloid leukemia factor 1 (Myelodysplasia-myeloid leukemia factor 1)	435	435 e-122
			AAA99997.1	t(3;5)(q25.1;p34) fusion gene	435	e-122
			AAH07045.1	AAH07045 myeloid leukemia factor 1	435	435 e-122
				unamed protein product	396	396 e-110
				unnamed protein product	383	383 e-106
NM_028784	Mm.17403 F:(C-IR)		CAC36886.1	bA525O21.1 (coagulation factor XIII, A1 polypeptide)	. 482	482 e-135
NP_083060.1		-2.01				
	·	·	1F13	A Chain A, Recombinant Human Cellular Coagulation Factor Xiii	482	e-135
			1F13 ·	B Chain B, Recombinant Human Cellular Coagulation Factor Xiii	482	e-135
	:		1GGT	A Chain A, Coagulation Factor Xiii (A-Subunit Zymogen) (B.C.2, 3.2, 13) (Protein-Glutamine Gamma-Glutamethraneferace A Chain)	482	482 e-135
			1GGT	B Chain B Coamlation Factor Xiii (A.Shhmit Zymogen) (R C 2 3 2 13) (Protein.	482	487 - 135
				Glutamine Gamma-Glutamyltransferase A Chain)	}	
:		:	1GGU	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	482	482 e-135
	:		1GGY	B Chain B, Human Factor Xiii With Ytterbium Bound In The Ion Site	482	e-135
			1QRK	B Chain B, Human Factor Xiii With Strontium Bound In The Ion Site	482	482 e-135
:	·		1GGY	A Chain A, Human Factor Xiii With Ytterbium Bound In The Ion Site	482	482 e-135
			1GGU ·· ·	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	482	482 e-135
: .			1QRK	A Chain A, Human Factor Xiii With Strontium Bound In The Ion Site	482	e-135
			XP 165833.1	similar to coagulation factor XIII, Alt polypeptide	482	482 e-135
			AAL12161.1	AF418272 1 coagulation factor XIII, A1 polypeptide	482	482 e-135
		:	AAA52415.1	factor XIII a subunit	481	481 e-135
			1EVU	A Chain A, Human Factor Xiii With Calcium Bound In The Ion Site	481	e-135
			1EVU ·	B Chain B, Human Factor Xiii With Calcium Bound In The Ion Site	481	e-135
· · · · · · · · · · · · · · · · · · ·		•	NP_000120.1	coagulation factor XIII.A1 subunit precursor; Coagulation factor XIII, A polypeptide;	481	e-135
		•		Tgase		
			AA:A52488.1	clotting factor XIIIa precursor (EC 2.3.2.13)	481	e-135
			P00488	F13A_HUMAN Coagulation factor XIII A chain precursor (Protein-glutamine gamma-glutamyltransferase A chain)	481	481 e-135
	: · · · ;		EKHUX	protein-glutamine gamma-glutamyltransferase (EC 2.3.2.13), plasma	481	e-135
	:	· ·	1FIE	B Chain B, Recombinant Human Coagulation Factor Xiii	481	481 e-135
; ;		; ;	LFIE .	A Chain A, Recombinant Human Cogenlation Factor Xiii	481	481 e-135

			т-	т-	т-	_	$\overline{}$	·	_		13	 	Ė		_		_	Ι				Г	Г	_	T ·	Т
101 0 125	25.	324 3E-88	3E-88	3E-88	324 3E-88	324 3E-88	324 3E-88	3E-88	3E-87	2E-86	7E-84	2E-81	2E-81	2E-76	1E-75	283 1E-75	1E-75	1E-75	1E-75	1E-75	1E-75	1E-75	7B-66	4E-64	244 4E-64	DAN AR GA
101	104,	324	324		324	324	324	324	321	318	310	301	301	285	283	283	283	283	283	283	283	283	250	244	244	244
factor XIII precursor	conmission forton VIII A 1 maleusanida	high-mobility group box 1; high mobility group box 1; high-mobility group (nonhistone chromosomal) protein 1	HMG1 HUMAN High mobility group protein 1 (HMG-1)	nonhistone chromosomal protein HMG-1	HMG-1 protein (AA 1-215)	on-histone chromatin protein HMG1	AAH03378 high-mobility group (nonhistone chromosomal) protein 1	high-mobility group (nonhistone chromosomal) protein 1	HMG-1	nonhistone chromosomal protein HMG-1	dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)	HM1X HUMAN High mobility group protein 1-like 10 (HMG-1L10)	bK445C9.3 (high-mobility group (nonhistone chromosomal) protein 1-like 10)	AC007277_1 similar to nonhistone chromosomal protein HMG-1 [Homo sapiens]; probable pseudogene; similar to P09429 (PID:g123369)	AAH00903 high-mobility group (nonhistone chromosomal) protein 2	high-mobility group box 2; high-mobility group (nonhistone chromosomal) protein 2	HMG2 HUMAN High mobility group protein 2 (HMG-2)	nonhistone chromosomal protein HMG-2	HMG-2	high mobility group 2 protein	AAH01063 high-mobility group (nanhistone chromosomal) protein 2	high mobility group protein 2	similar to dJ579F20.1 (high-mobility group (nonhistone chromosomal) protein 1-like 1)	high-mobility group box 3; high-mobility group (nonhistone chromosomal) protein 4	HMG4_HUMAN High mobility group protein 4 (HMG-4) (High mobility group protein 2a) (HMG-2a)	high mobility groum anotein 2.
AAA52489.1	A A H27062 1	NP_002119.1	P09429	S02826	CAA31110.1	AAB08987.1	AAH03378.1	AAH30981.1	BAA09924.1	S29857	CAB92731.1	O9UGV6	CAB62951.1	AAF19244.1	AAH00903.2	NP_002120.1	P26583.	NSHUH2	- CAA44395.1	AA:A58659.1	AAH01063.1	2001363A	XP_086648.2	NP_005333.1	015347	CA A 71142 1
		F:(C-IR)				•					;				1	: .				بريد		•				
		Mm.16421 F:(C-IR)				•								,				, .:		· · · · · · · · · · · · · · · · · · ·		:		•	**	
		NM_010439 NP_034569.1																			: :	7				

		- 1				
NM_013459 NP_038487.1	Mm.4407 F:(C-IR)		P00746	CFAD_HUMAN Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adinsin)	370	370 e-102
.;. 1.*	•		. · .			
			CAC48304.1	adipsin/complement factor D precursor	358	358 4E-99
			DBHU	complement factor D (BC 3.4.21.46) precursor [validated]	352	352 SE-97
		1	IFDP	A Chain A, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340	340 1E-93
			1FDP	B Chain B, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340	340 1E-93
	:		1FDP	D Chain D, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	340	1E-93
	; ;		1FDP · · ·	C Chain C, Proenzyme Of Human Complement Factor D, Recombinant Profactor D	.340	340 1E-93
: ,			AAH34529.1	Unknown (protein for IMAGE:4780594)	340	1E-93
			1DST	Mutant Of Factor D With Enhanced Catalytic Activity	330	1E-90
			1BIO	Human Complement Factor D In Complex With Isatoic Anhydride Inhibitor	329	4E-90
	·		IDIC · · ·	A Chain A, Structure Of 3,4-Dichloroisocoumarin-Inhibited Factor D	329	4E-90
			1DSU	A Chain A, Human Factor D, Complement Activating Enzyme	329	4B-90
			1HFD	Human Complement Factor D In A P21 Crystal Form	329	4E-90
			1DFP	A Chain A, Factor D Inhibited By Diisopropyl Fluorophosphate	329	329 4E-90
		·	1DFP	B Chain B, Factor D Inhibited By Diisopropyl Fluorophosphate	329	329 4E-90
·			1DSU	B Chain B, Human Factor D, Complement Activating Enzyme		329 4E-90
1	:		XP_084037.1	similar to Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)		328 8E-90
			NP 001919.1	adipsin/complement factor D precursor	324	1E-88
			AAA35527.1	adipsin/complement factor D	324	
AK017926	Mm.21697 F:(C-D)	F:(C-D) -	NP_061931.1	RTP801	372	e-103
BAB31006.1		: :				
:			BAA91214.1	unnamed protein product	372	e-103
			AAH07714.1	hypothetical protein	372	372 e-103
			AAH15236.1	hypothetical protein	372	372 e-103
			AAL38424.1	RTP801	372	372 e-103
			AAM10442.1	REDD-1.	372	e-103
			CAB66603.1	hypothetical protein	370	370 e-102

T								0	9	9	9	9		L	9	2	٠.				1						
	e-10(364 e-100.	364 e-100	364 e-100	364 e-100	364 e-100	361 e-100	360 3E-99	359 4E-99	350 3E-96	317 e-136	•	e-136	e-136	e-135	e-135	0		0	0	0	0	0	0	0	0
	364 e-100		364	364	364	364	364	361	360	359	350	317	:	317	317	313	313	11960		1196 0	119610	11960	11960	1196 0	1195	1195	1023 0
	suppressor of cytokine signaling-2; STAT induced STAT inhibitor-2; cytokine-inducible SH2 protein 2		similar to Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	SOC2_HUMAN Suppressor of cytokine signaling 2 (SOCS-2) (Cytokine-inducible SH2 protein 2) (CIS-2) (STAT induced STAT inhibitor 2) (SSI-2)	STAT induced STAT inhibitor-2	STAT-induced STAT inhibitor-2	STAT induced STAT inhibitor-2	STAT induced STAT inhibitor 2	cytokine-inducible SH2 protein 2	CIS2	suppressor of cytokine signalling-2; HSSOCS-2	unknown		similar to SET domain and mariner transposase fusion gene		SET domain and mariner transposase fusion gene	orf, encodes putative chimeric protein with SET domain in N-terminus with similarity to several other human, Drosophila, nematode and yeast proteins	$\overline{}$		TFR1_HUMAN Transferrin receptor protein 1 (TR1) (TR) (TR) (Trft) (CD71 antigen)	transferrin receptor	put. transferrin receptor (aa 1-760)	transferrin receptor	transferrin receptor.	AF187320 1 transferrin receptor	AAH01188 transferrin receptor (p90, CD71)	C Chain C, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor
	Mm.4132 F:(C-D) - NP_003868.1	: !	XP_170547.1	014508	BAA22429.1	AAC34745.1	AAH10399.1	JC5626	JC5760	BAA22536.1	AAC98896.1	AAC09350.1	: : : · .	XP 057054.6	H11635	NP 006506.1	AAC52012.1	NP_003225:1		P02786	JXHU	CAA25527.1	AAA61153.1	1011297A	AAF04564.1	AAH01188.1	1DE4
	F:(C-D) -		· 1					مندم				F:(C-D)-	2.02						2.02				·				
	Mm.4132	·		\								Mm.56539			1.			Mm.26069	:								. :
	NM_007706	NP 031732.1							:			AK017895	XP 1326921					NM_011638	NP_035768.1							·	

	224 6B-58	similar to folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	XP_165392.1			
	228 3E-59	prostate-specific membrane antigen	AAM34479.1			. `
	228 3B-59	AF176574 1 folylpoly-gamma-glutamate carboxypeptidase	AAD51121.1		1.1	:
	228 3E-59	prostate, specific membrane antigen	AAA60209.1			
	228 3E-59	prostate-specific membrane antigen.	A56881	`1 !		. V. Y
		glutamate carboxypeptidase) (FGCP) (Folate hydrolase 1) (Prostate-specific membrane antigén) (PSMA) (PSM)	•			
		carboxypeptidase) (mGCP) (N-acetylated-alpha-linked acidic dipeptidase I) (NAALADase I) (Pteroylpoly-gamma-glutamate carboxypeptidase) (Folylpoly-gamma-	· . · . · . · . · . · . · . · . · . · .		+ 2	
	228 3B 50	Process Included and Sold Figure 1 (Membrane of Internate Carboxymentidase II (Membrane of Internate	004609			
	228 3E-59	folate hydrolase (prostate-specific membrane antigen) 1; folate hydrolase 1 (prostate-specific membrane antigen)	NP_004467.1	: :		•
	228 2E-59	prostate-specific membrane antigen	AAC83972.1			•
	315 2E-85	unnamed protein product	BAA91153.1	: ,		
14	Γ	transferrin-recentor2	AAC78796.1			
_13	T	transferrin receptor 2	NP 003218.1	:		
	545 e-154	AF067864 1 transferrin receptor 2 alpha	AAD45561.1			
	545 e-154	TFR2 HUMAN Transferrin receptor protein 2 (TfR2)	Q9UP52			
	1020 0	H Chain H, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8		,	
	1020 0	G Chain G, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
	1020 0	F Chain F, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8	1		
	1020 0	E Chain E, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8 ·			
	1020 0	D Chain D, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			-
	1020 0	C Chain C, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
	1020 0	B Chain B, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8			
	1020 0	A Chain A, Crytal Structure Of The Ectodomain Of Human Transferrin Receptor	1CX8 ·		:	
	1023 0	I Chain I, Hemochromatosis Protein Hfe Complexed With Transferrin Receptor	1DE4			
	0 (701					
	1000	R Chain B Hamonthrain Drotain Uto Commland With Tourstain Dronte	1mg/			

400	0	0	0	135	178	169	164	-153	-153	-126 e-93	0	00
E.	835		745	623 e-178	623 e-178	594 e-169	575 e-164	541 e-153	541 e-153	450 e-126 340 5e-93	765	759
ingenigiliv evergenden geben er er er er men i vessenden i vessenden er	60kDa BRG-1/Brm associated factor subunit c isoform 2	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d3; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60C; Swp73-like protein; chromatin remodeling complex BAF60C subunit; SWI/SNF complex 60 kDa subunit C	SWI/SNF complex 60 KDa subunit	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1 isoform a; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit, Swp73-like protein; SWI/SNF complex 60 kDa subunit A	SMARCD1 protein SM//SME-related matrix-associated actin-dependent requilator of chromatin D1	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d2; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60B; Swp73-like protein; chromatin remodeling complex BAF60B subunit, SWI/SNF complex 60 kDa subunit B	SWI/SNF complex 60 KDa subunit SWI/SNF-related matrix-associated actin-dependent regulator of chromatin d1	isoform b; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 60A; chromatin remodeling complex BAF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit A	SWI/SNF complex 60 KDa subunit	unknown	alpha 1 actin precursor, alpha skeletal muscle actin	cardiac muscle alpha actin proprotein; smooth muscle actin alpha 2 actin; alpha-cardiac actin
	AAR88510.1	NP_003069.2	AAC50697.1	NP_003067.2	AAH09368.2 AAD23390 1	NP_003068.2	AAC50696.1	NP_620710.1	AAC50695.1	AAS02031.1 · AAS00380.1	NP_001091.1	NP_005150.1 NP_001604.1
	F:(C-D) -1.70									·	F:(C-D) -1.69	
ča jo provi ileta nimili: "Ori itekan	Vlm.279751										Mm.214950	·
mitorus ergeni meters ofinalis	025891 080167.2 Mm.27								· :	· :	M12866 AAA37164.1 N	· · ·

ATHUSM actin alpha 2 aortic smooth muscle , human	750	
NP_U01606.1 actin, gamma 2 propeptide; actin, alpha-3	748 0	·
NP_001605.1 26; deafness, autosomal dominant 20; cytoskeletal gamma-actin	721 0	_
•	724	
302 4 P.	0 121	
	0 . 02/	_
AAH16045.1 Beta actin	718 0	_
CAA45026.1 mutant beta-actin (beta'-actin)	. 716 .0	
AAH08633.1 actin beta	746 0	
	0 0 017	
	0 10/	
AAH12854,1 ACTB protein	0 669	
XP_293924.1 similar to RIKEN cDNA 4732495G21 gene	0 989	
XP 371558.2 similar to FKSG30	670 0	
	0,00	
٠	0 600	
AAG50355.1 . FKSG30	0 899	
XP_372957.1 similar to FKSG30	0 999	
XP_292982.4 similar to pote protein; Expressed in prostate, ovary, testis, and placenta	999	
	650 0	
0902248A actin beta related pseudogene	571 e-162	
AAH23548.1 ACTG1 protein	504 e-142	
))) i	
AAA51580.1 gamma-actin	443 e-124	
AAH06372.1 ARP1 actin-related protein 1 homolog B, centractin beta	430 6-120	
ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1		
_		
NP_005726.1 yeast homolog B	430 e-120	
ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related		٠.
INT_oub/21.1 certuosome-associated acun nomotog; ARP1, yeast nomotog A	423 e-118	
1818358A actin-related protein	421 e-117	
		_

actin alpha 2, aortic smooth muscle

ATHUSM

NP 005150.1	cardiac muscle alpha actin proprotein; smooth muscle actin	755	0
NP 001606.1	actin, gamma 2 propeptide; actin, alpha-3	754	0
NP_001091.1	alpha 1 actin precursor; alpha skeletal muscle actin	753	0
. i	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant		
NP_001605.1	26; deafness, autosomal dominant 20;	724	0
JC5818	gamma-actin	724	0
NP_001092.1	beta actin; beta cytoskeletal actin	724	0
AAH16045.1	Beta actin	722	0
CAA45026.1	mutant beta-actin (beta'-actin)	720	0
AAH08633.1	actin, beta	719	<u></u>
AAH12854.1	ACTB protein	703	0
AAH17450.1	Unknown (protein for IMAGE:3538275)	707	0
XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	689	0
XP_371558,2	similar to FKSG30	210	0
XP_065237.5	similar to FKSG30	671	0
AAG50355.1	FKSG30	671	0
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	899	0
XP_372957.1	similar to FKSG30	899	0
AAA51586.1	actin prepeptide	. 661	0
0902248A			
.:	actin deta related pseudogene	575 e-163	<u>8</u>
AAH23548.1	ACTG1 protein	506 e-143	43
AAA51580.1	gamma-actin	445 e-124	24
AAH06372.1	ARP1 actin-related protein 1 homolog B, centractin beta	431 e-	e-120
• • • • • • • • • • • • • • • • • • • •	ARP1.actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 (actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast		
NP_005726.1	homolog B	429 e-120	120
	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV;		
NP_005727.1		422 e-118	18
1818358Å	actin-related protein	421 e-117	117
	Actin related protein M1	387 e-107	107
			•

	NP_115876.2	actin related protein M1	382 e-105
	AAH07289.1	Actin related protein M1	382 e-105
•	CAA57692.1	beta-centractin	380 e-105
•	NP_612146.1	actin-related protein T1	369 e-102
	AAM00432.1	actin-related protein T1	369 e-102
·	NP_536356.3	actin-related protein M2, actin-related protein hArpM2; actin-related protein T2	369 e-102
•	BAB85862.1	actin-related protein hArpM2	367 e-101
	AAP20055.1	HSD27	366 e-101
	AAH29499.1	Actin-related protein M2	365 e-100
	NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	356 6e-98
٠	AAH14546.1	Actin-related protein 2	353 5e-97
•	~ NP_006678.1	actin-like 7A; actin-like 7-alpha	328 2e-89
•	XP_208204.1	similar to actin-related protein 2	326 7e-89
. ,	XP_377904.1	similar to cytoplasmic beta-actin	325 2e-88
. ,	AAP37280.1	actin alpha 1 skeletal muscle protein	323 6e-88
	AAH10417.2	ACTG1 protein	323 8e-88
•	AAH36253,1	ACTR2 protein	318 16-86
·.	NP_006677.1	actin-like 7B; actin-like 7-beta	316 9e-86
•	AAH09544.1	Unknown (protein for IMAGE:3897065)	311 26-84
	BAB71690.1	unnamed protein product	303 6e-82
•	NP_848620.1	actin-like	303 8e-82
	AAP20052.1	HSD21	301 2e-81
F:(C-D)			.168
3484.1 Mm.5316 -1.46	-1.46 NP_001095.1	skeletal muscle specific actinin, alpha 3	
	· · ·		144
•	NP_001094.1	actinin, alpha 2	
:			141
, !	NP_001093.1	actinin, alpha 1	0
I			.140
•	FAHUAA	aipha-actinin 1 - human	0 /
•	: • • • • • • • • • • • • • • • • • • •		134
	NP_004915.2	actinin, alpha 4	8.

b And A 4 Andrews Andr	134
٠.,	0 10
AAC17470.1 alpha actinin	0
AAH15620.2 ACTN4 protein	924 0
CAA38970.1 alpha-actinin	0 · 668
CAD62344.1 unnamed protein product	0 698
1HCl_A Chain A, Crystal Structure Of The Rod Domain Of Alpha-Actinin	753 0
1HCI_B Chain B, Crystal Structure Of The Rod Domain Of Alpha-Actinin	753 0
XP_293669.4 similar to actinin, alpha 4	497 e-140
spectrin, beta, non-erythrocytic 1 isoform 2; Spectrin, beta, nonerythrocytic-1 NP_842565.1 (beta-fodrin)	426 e-118
spectrin, beta, non-erythrocytic 1 isoform 1; Spectrin, beta,nonerythrocytic-1 NP_003119.1 (beta-fodrin)	426 e-118
NP_008877.1 spectrin, beta, non-erythrocytic 2	415 e-115
AAA60578.1 spectrin Rouen (beta-220-218) mutant coding sequence	405 e-112
spectrin, beta, erythrocytic (includes spherocytosis, clinical type I); Spectrin, beta, NP_000338.2 erythrocytic; spectrin, beta, erythrocytic (includes sperocytosis, clinical type I)	405 e-112
SPCB_HUMA N Spectrin beta chain, erythrocyte (Beta-I spectrin)	405 e-112
AAQ14859.1 beta spectrin IV	399 e-110
AAG42473.1 spectrin beta IV	399 e-110
NP_066022.1 spectrin, beta, non-erythrocytic 4 SPCQ_HUMA Spectrin beta chain, brain 3 (Spectrin, non-erythroid beta chain 3)(Beta-IV	399 e-110
NP_079489.1 spectrin, beta, non-erythrocytic 4	396 e-110
AAF93171.1 betalV spectrin isoform sigma2	396 e-110

394 e-109	. 707	3/9 e-104	344 5e-94	264 7e-70	264 7e-70	259 2e-68	245 36-64	245 3e-64	245 39-64	245 36-64		245 36-64	245 3e-64	245 3e-64	245 3e-64	245 3e-64	241 46-63	231 4e-60	231 4e-60	231 4e-60	224 8e-58
AAF93173.1 betalV spectrin isoform sigma4	. :	TOOU_A Appra-Actinin	NP_057726.1 spectrin, beta, non-erythrocytic 5; beta V spectrin	AAB41498.1 alpha II spectrin	AAH53521.1 SPTAN1 protein	NP_003118.1 spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	plectin 1 isoform 1; hemidesmosomal protein 1; epidermolysis bullosa simplex 1		782.1		٠.	NP_958784.1 (Ogna)	piectin 1 isoform 11; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958786.1 (Ogna)	plectin 1 isoform 3; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP_958781.1 (Ogna)	plectin 1 isoform 2; hemidesmosomal protein 1; epidermolysis bullosa simplex 1 NP 958780.1 (Ogna)	NP_958783.1 (Ogna) PI F1 HI IMA	N Plectin 1 (PLTN) (PGN) (Hemidesmosomal protein 1) (HD1)	_	BPA1_HUMA Bullous pemphigoid antigen 1 isoforms 1/2/3/4/5/8 (230 kDa bullous pemphigoid National plaque protein) (Dystonia musculorum protein)	bullous pemphigoid antigen 1 isoform 1; bullous pemphigoid antigen 1 NP_899236.1 (230/240kD); dystonin; hemidesmosomal plaque protein	MACF_HUMA Microtubule-actin crosslinking factor 1, isoforms 1/2/3 (Actin cross-linking family N protein 7) (Macrophin 1) (Trabeculin-alpha) (620 kDa actin-binding protein)

	BAA83821.1	actin binding protein ABP620	224 8e-58	9-58
		microfilament and actin filament cross-linker protein isoform a; 620 kDa actin binding protein; actin cross-linking factor; macrophin 1; trabeculin-alpha; actin		
:	NP_036222.3	cross-linking family protein 7	224 8	86-58
	AAF06360.1	trabeculin-alpha	223 2	2e-57
	S66292 ···	actin-crosslinking protein ACF7 - human (fragment)	215 3	3e-55
. •	1MB8_A	Chain A, Crystal Structure Of The Actin Binding Domain Of Plectin	211 7	7e-54
	CAA60503.1	alpha-spectrin	203 1	16-51
NM_026369 F:(C-D			•	
NP_080645.1 Mm.288974 -1.38 NP_005708.1	AAH57237.1	actin related protein 2/3 complex subunit 5; Arp2/3 protein complex subunit p16 ARPC5 protein	293 8 285 1	8e-79
	AAP97155.1	ARC16-2		4e-54
	NP_112240.1	actin related protein 2/3 complex, subunit 5-like	210 5	5e-54
NM_018817 F:(C-D)		SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121	
NP_061287.1 Mm.2742321.37	NP_054859.2	1; HepA-related protein; SMARCA-like protein 1	დ	0
	• • • • • • • • • •	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin a-like	121	
	AAH16482.1.		0	0
	· •		120	
•••	AAF24984.1	HepA-related protein HARP	S	0
			112	
•	T34557	hypothetical protein DKFZp434B1050.1 - human (fragment)	ß	0
	BAA90955.1	unnamed protein product	975	0
	.BAC04536.1	unnamed protein product	220 4	1e-56
NM 026552 F.(C-D			:	
NP_080828.1 Mm.289306 -1.35 NP_005709.	"NP_005709.1	actin related protein 2/3 complex subunit 4; Arp2/3 protein complex subunit p20	326 5e-89	68-9
	AAH12596.2	ARPC4 protein	322, 16-87	e-87
AF316037 F:(C-D		actin-binding LIM protein 1 isoform a; LIM actin-binding protein 1; limatin;	130	_
NP_848803.2 Mm.244618 -1.35 N	NP_002304.2	actin-binding LIM protein	7	.0
			130	
	AAC51676.1	actin-binding double-zinc-finger protein	Ω.	<u>o</u>
			127	
	BAA06681.2	KIAA0059	~	-

2005/082398	1.12					PCT	/US	2005	5/0055	596		
111 3 0 756 0 651 0 651 0 518 e-146 508 e-143 506 e-143 433 e-121	143_ 0 6		561 e-160 430 e-120	755 0	753 0	709 0	0 802	616 e-176	425 e-118	425 e-118	425 e-118	424 e-118
actin-binding LIM protein 1 isoform m; LIM actin-binding protein 1; limatin; actin-binding LIM protein actin-binding LIM protein 1 isoform s; LIM actin-binding protein 1; limatin, actin-binding LIM protein KIAA0843 protein actin binding LIM protein family, member 3 Unknown (protein for IMAGE:6188753) KIAA1808 protein actin binding LIM protein family, member 2 unnamed protein product ABLIM1 protein	uncharacterized hypothalamus protein HARP11	unnamed protein product	unnamed protein product unnamed protein product	ARP1 actin-related protein 1 homolog A, centractin alpha; ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha); centractin alpha; actin-RPV; centrosome-associated actin homolog; ARP1, yeast homolog	actin-related protein	ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1 (actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast homolog B	ARP1 actin-related protein 1 homolog B, centractin beta	beta-centractin	actin, gamma 1 propeptide; actin, cytoplasmic 2; deamess, autosomal dominant 26; deafness, autosomal dominant 20;	gamma-actin gamma-actin	cardiac muscle alpha actin proprotein; smooth muscle actin	beta actin; beta cytoskeletal actin
NP_006710.2 NP_006711.2 BAA74866.2 NP_05560.1 AAH67214.1 BAB47437.1 NP_115808.2 BAC04414.1 AAH02448.1	F:(C-D) -1.32 NP_060947.1 BAA04243.4	BAB14083.1	CAD62610.1 CAD61940.1)) NP_005727.1	1818358A	NP_005726.1	AAH06372.1	CAA57692.1	NP_001605.1	JC5818	NP 005150.1	NP_001092.1
	F:(C-E		·	F:(C-D) -1.31		. ·	•		•		•	
:	019785 062759.1 Mm.29317	· ·		Mm.3118	•							
,	UM_019785 UP_062759.1			NM_016860 NP_058556.1 Mm.3118								

AAH08633.1	actin. beta	424 e-118
i coccosi in a		
AAH16045.1	Beta actin	424 e-118
· CAA45026.1	mutant beta-actin (beta'-actin)	423 e-118
NP_001091.1	alpha 1 actin precursor, alpha skeletal muscle actin	423 e-118
NP_001604.1	alpha 2 actin; alpha-cardiac actin	422 e-117
NP_001606.1	actin, gamma 2 propeptide; actin, alpha-3	422 e-117
ATHUSM	actin alpha 2, aortic smooth muscle	422 e-117
XP_293924.1	similar to RIKEN cDNA 4732495G21 gene	417 e-116
AAH17450.1	Unknown (protein for IMAGE:3538275)	410 e-114
AAH12854.1	ACTB protein	408 e-113
AAG50355.1	FKSG30	408 e-113
XP_065237.5	similar to FKSG30	408 e-113
XP_371558.2	similar to FKSG30	404 e-112
XP_292982.4	similar to pote protein; Expressed in prostate, ovary, testis, and placenta	404 e-112
XP_372957.1	similar to FKSG30	404 e-112
AAA51586.1	actin prepeptide	355 2e-97
0902248A		
	actin beta related pseudogene	330 6e-90
NP_005713.1	actin-related protein 2; ARP2 (actin-related protein 2, yeast) homolog	322 2e-87
AAH14546.1	Actin-related protein 2	318 26-86
NP_115876.2	actin related protein M1	314 6e-85
ARM1_HUMA		•••
Z	Actin related protein M1	314 6e-85
NP_536356.3	actin-related protein M2; actin-related protein hArpM2; actin-related protein T2	309 1e-83
AAH07289.1	Actin related protein M1	309 2e-83
BAB85862.1	actin-related protein hArpM2	308 2e-83
AAH29499.1	Actin-related protein M2	307 7e-83
AAH23548.1:	ACTG1 protein	297 6e-80
XP_208204.1	similar to actin-related protein 2	296 1e-79
NP_612146.1	actin-related protein T.1	295 4e-79

648 644

protein, 1A; coronin-1

NP_009005.1

AAA77058.1

coronin-fike protein

KIAA0925 protein

BAA76769.1

412 e-114

coronin, actin binding protein, 2B; clipin C; coronin, actin-binding, 2B; coronin,

actin-binding protein, 2B

CO2B_HUMA

NP_006082.1

Coronin 2B (Coronin-like protein C) (ClipinC) (Protein FC96)

409 e-113

411 e-114

	NP_438171.1	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein 2; WD protein IR10	408 e-113
	NP_003380.2	coronin, actin binding protein, 2A; coronin, actin-binding protein, 2A; coronin 2A; coronin-like protein B; WD-repeat protein2; WD protein IR10	408 e-113
	AAB47807.1	WD protein IR10	404 e-112
	T47174	hypothetical protein DKFZp762l166.1 - human (fragment)	389 e-107
	AAS48630.1	unknown	314 7e-85
	NP_116243.1	hypothetical protein FLJ14871	311 56-84
	AAQ04659.1	Unknown	311 6e-84
	NP_078811.1	hypothetical protein FLJ22021	234 6e-61
	D) NP_001094.1		. 171
	NP 001095.1	skeletal muscle specific actinin alnha 3	141
			7 021
	NP_001093.1	actinin, alpha 1	4 0
•	FAHUAA	alpha-actinin 1 - human	139 1 0
	NP 0049152	actinin plane 4	136
	2:010t00_ INT		
	BAA24447.1	alpha actinin 4	136 1 0
	AAC17470 1	alpha actinin	126
٠	AAH15620.2	ACTN4 protein	
	1HCI A	Chain A, Crystal Structure Of The Rod Domain Of Alpha-Actinin	891
•	· 1HCI_B	Chain B, Crystal Structure Of The Rod Domain Of Alpha-Actinin	
	CAA38970.1	alpha-actinin	0 . 288
	CAD62344.1	unnamed protein product	835 0
•	XP_293669.4	similar to actinin, alpha 4	524 e-148
•	•		•

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4	١

Chain A, Crystal Structure Of Two Central Spectrin-Like Repeats From	455 e-127
NP_008877.1 spectrin, beta, non-erythrocytic 2	412 e-114
spectrin, beta, non-erythrocytic 1 isoform 2; Spectrin, beta, nonerythrocytic-1 NP_842565.1 (beta-fodrin)	408 e-113
spectrin, beta, non-erythrocytic 1 isoform 1; Spectrin, beta, nonerythrocytic-1 NP_003119.1 (beta-fodrin)	407 e-113
spectrin, beta, erythrocytic (includes spherocytosis, clinical type I); Spectrin, beta, NP 000338.2 erythrocytic; spectrin, beta, erythrocytic (includes sperocytosis, clinical type I)	391 e-108
SPCB_HUMA N Spectrin beta chain, erythrocyte (Beta-I spectrin)	391 e-108
AAA60578.1 spectrin Rouen (beta-220-218) mutant coding sequence	391 e-108
AAG42473.1 spectrin beta IV	381 e-105
NP_066022.1 spectrin, beta, non-erythrocytic 4	381 e-105
SPCQ_HUMA Spectrin beta chain, brain 3 (Spectrin, non-erythroid beta chain 3)(Beta-IV N	381 e-105
AAQ14859.1 beta spectrin IV	381 e-105
NP_079489.1 spectrin, beta, non-erythrocytic 4	375 e-103
AAF93171.1 betalV spectrin isoform sigma2	375 e-103
AAF93173.1 betalV spectrin isoform sigma4	373 e-103
NP_057726.1 spectrin, beta, non-erythrocytic 5; beta V spectrin	322 2e-87
•	284 5e-76
AAH53521.1 SPTAN1 protein	284 5e-76
NP_003118.1 spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	279 2e-74
CAA60503.1 alpha-spectrin	231 5e-60

210 1e-53	209 26-53	st) 850 0	793		597 e-170	348 36-95	344 46-94	253 8e-67	252 2e-66	249 2e-65	248 36-65	248 3è-65		· 248 4e-65	248. 4e-65	. 248 5e-65	247 6e-65	247 8e-65	247 8e-65	246 1e-64	246 16-64	246 2e-64	245 3e-64	239 26-62	ARP1	/east
Spectrin alpha chain, erythrocyte (Erythroid alpha-spectrin)	actin-crosslinking protein ACF7 - human (fragment)	ARP3 actin-related protein 3 homolog; ARP3 (actin-related protein 3, yeast) homolog	actin-related protein 3-beta; actin-related protein 3-beta; actin-related protein Arp11; actin-related protein Arp11	actin related protein ARP4	ARP3BETA protein	similar to actin-related protein Arp11	actin-related protein Arp11 - human	FKSG74	FKSG72	FKSG73	Beta actin	beta actin; beta cytoskeletal actin	actin, gamma 1 propeptide; actin, cytoplasmic 2; deafness, autosomal dominant	26; deafness, autosomal dominant 20; cytoskeletal gamma-actin	gamma-actin - human	alpha 1 actin precursor; alpha skeletal muscle actin	mutant beta-actin (beta'-actin)	actin, bëta	cardiac muscle alpha actin proprotein; smooth muscle actin	similar to RIKEN cDNA 4732495G21 gene	actin alpha 2, aortic smooth muscle - human	alpha 2 actin; alpha-cardiac actin	actin, gamma 2 propeptide; actin, alpha-3	nknown (protein for IMAGE:3538275)	ARP1 actin-related protein 1 homolog B, centractin beta; centractin beta; ARP1	(actin-related protein 1, yeast) homolog B (centractin beta); PC3; ARP1, yeast
SPCA_HUMA N	S66292	712.1	<u>~</u>	_	AAH15207.1	XP_374583.1	JC7580-	AAK31778.1	AAK31776.1	AAK31777.1	AAH16045.1	. NP_001092.1	1	<u>-</u> ;	JC5818	NP_001091.1	CAA45026.1	AAH08633.1	NP_005150.1	XP_293924.1	ATHUSM	<u> </u>	NP_001606.1	AAH17450.1		

SWU/SNF-related matrix-associated actin-dependent regulator of chromatin d1 soform at Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 604.; chromatin remodeling complex BRG1-associated rection 605.2 SWI/SNF complex 60 kDa subunit and complex BRG1-associated actin-dependent regulator of chromatin D1 SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin D1 soform b; Rsc6p; mammalian chromatin remodeling complex BRG1-associated factor 604; chromatin remodeling complex BRF60A subunit; Swp73-like protein; SWI/SNF complex 60 kDa subunit AAS00380.1 SWI/SNF complex 60 kDa subunit AAS00380.1 unknown AAS00380.1 unknown AAS00380.1 unknown AAS00380.1 actin related protein 2/3 complex subunit 1A; actin binding protein AAF00450.1 PRC02451 actin related protein 2/3 complex subunit 1A (S0P2-like protein) actin related protein 2/3 complex subunit 1A (A1 kD) actin-related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex subunit 1A (41 kD) actin related protein 2/3 complex, subunit 1A (41 kD) actin related protein 2/3 complex, subunit 1A (41 kD) actin related, matrix associated, actin dependent regulator of chromatin subfamily B member 1 (Integrase interactor 1 protein) (inSNF5) (BAF47) actin mamed protein product CAA09759.1 Initb BAB14784.1 unnamed protein product	44 47 47 48 47 4 47 4 47 4 47 4 47 4 47	v of chromatin d1 x BRG1-associated Swp73-like protein; 589 e-168 tor of chromatin D1 582 e-165 x BRG1-associated Swp73-like protein; 505 e-142	505 e-142	366 e-100	261 5e-69	159 2e-38	730		ein) 723 0 complex subunit	533 e-151 257 25 08	3	754 0	or of chromatin 5) (BAF47) 749 0	!	710 0	
0 - 04 - 04	0 7 7 0 7	VINNE-related matrix-associated actin-dependent regulator form a; Rsc6p; mammalian chromatin remodeling complex to 60A; chromatin remodeling complex BAF60A subunit; SII/SNF complex 60 kDa subunit A VI/SNF-related, matrix-associated, actin-dependent regulate form b; Rsc6p; mammalian chromatin remodeling complex tor 60A; chromatin remodeling complex tor 60A; chromatin remodeling complex BAF60A subunit; SII/SNF complex 60 kDa subunit A	///SNF complex 60 KDa subunit	chown	rnown	ARCD2 protein O2451	in related protein 2/3 complex subunit 1A; actin binding pro hizosaccharomyces pombe sop2-like); SOP2-like protein	in related anatolic of the second in the second in	in related protein 2/3 complex subunit 1B; ARP2/3 protein of	I; actin related protein 2/3 complex, subunit 1A (41 kD) mown	///SNF related, matrix associated, actin dependent regulato viamily b, member 1; sucrose nonfermenting, veast, homol	sractor 1	///SNP related, matrix associated, actin dependent regulato vfamily B member 1 (Integrase interactor 1 protein) (hSNF5	Q	named protein product	F5/INI1 protein
	F.(C-D) Wm.34695 -1.18 Wm.279751 -1.14	0			•		. 0			:	:	<u>م</u> د	_	••	-;	· ·

WO 2005/082398 PCT/US2005/005596

152

Subtable 1B: Wholly Unfavorable Genes and Proteins

		.]			•	
	Unigene	Behavior	Human Proteins	Human Protein Name	Score (bits)	E-value
NM_007588 NP_031614.1	Mm.4642	U:(IR-D) 3.8	AAC50300.1	calcitonin receptor	758	
1 .	· 10.		BAA86929.1	calcitonin receptor	758	
			BAA86928.1	calcitonin receptor	758	0
			NP_001733.1	calcitonin receptor	754	0
	1		I37217 .	calcitonin receptor	754	Ó
	1		CAA49541.1	human calcitonin receptor	754	0
	, , , , ,		CÀA57849.1	truncated isomer of calcitonin receptor	754	0
		·	AAB83945.1.	Calcitonin Receptor, alternatively spliced form	754	0
				CALR_HUMAN Calcitonin receptor precursor (CT-R)	748	0
			S34486	calcitonin receptor	748	0
	·		AAA35640.1	calcitonin receptor	748	0
	•		AAB83944.1	Calcitonin Receptor, alternatively spliced form	744	0
. [1		AAC50301.1	calcitonin receptor isoform	731	0
::			NP 005786.1	calcitonin receptor-like	511	e-144
: 1			Q16602	CGRR_HUMAN Calcitonin gene-related peptide type 1 receptor precursor (CGRP type 1 receptor)	511	6-144
- 1			JC2477	calcitonin receptor-like protein	511	e-144
- 1			AAA62158.1	calcitonin-like receptor	511	e-144
T			AAC41994.1	CGRP type 1 receptor	511	
. [•		NP 000307.1	parathyroid hormone receptor 1	237	1e-61
1			Q03431	PTRR_HUMAN Parathyroid hormone/parathyroid hormone-related peptide receptor precursor (PTH/PTHR receptor)	237	1e-61
			A49191	parathyroid hormone/PTH-related peptide receptor	237	
			!!			

, ;			AAA36525.1	parathyroid hormone receptor	237	16-61
			1	parathyroid hormone receptor	237	1e-61
	·	: • :	AAA56774.1	parathyroid hormone/parathyroid hormone related peptide receptor	· 237	1e-61
		: :	AAB60657.1	parathyroid hormone/PTH-related peptide receptor	237	1e-61
	:		2119172A	parathyrin receptor	237	1e-61
	: { ! : • ; : • ;		Q13324	CRF2_HUMAN Corticotropin releasing factor receptor 2 precursor (CRF-R.2) (CRF2) (Corticotropin-releasing hormone receptor 2) (CRH-R.2)	221	6e-57
	•	:	AAC71653.1.	corticotropin-releasing factor receptor	221	6e-57
;			BAC05922.1	seven transmembrane helix receptor	221	6e-57
9 (A) A			AAB94503.1	corticotropin releasing hormone receptor type 2 beta isofor	221	8e-57
			AAB94562.1	corticotropin releasing hormone receptor type 2 gamma isoform; CRH type 2 gamma receptor	220	16-56
		•	AAC71654.1	corticotropin releasing hormone receptor type 2 gamma isoform; match to AF019381 (PID:g2738889)	220	1e-56
AK007657			· .			
	Mm 45138	U:(IR-D)	NP 115744.2	lencine zinner and CTNNRIP1 domain containing	302	. 0
			_	Leucine zipper & ICAT homologous protein LZIC	305	96-83
AK007999		(٠.	
BAB25399.1	Mm.35718 3.3	U:(цк-IJ) 3.3	XP 114275.1	similar to RIKEN cDNA 2010001C09	244	16-64
AF282730 AAF97239.1	U;(II) Mm.36851: 2.78	U:(IR-D) 2.78	NP_003247.1	tissue inhibitor of metalloproteinase 4 precursor	409	e-114
			Q99727	TIM4_HUMAN Metalloproteinase inhibitor 4 precursor (TIMP-4) (Tissue inhibitor of metalloproteinases-4)	409	e-114
			AAB40391.1	tissue inhibitor of metalloproteinase 4	409	e-114
			AAC34422.1	tissue inhibitor of metalloproteinase 4	409	e-114
	•		AAH10553.1	AAH10553 tissue inhibitor of metalloproteinase 4.	409	e-114
· .	!		NP 003246.1	tissue inhibitor of metalloproteinase 2 precursor	216	3e-56

		100				
	·		P16035	TIM2_HUMAN Metalloproteinase inhibitor 2 precursor (TIMP-2) (Tissue inhibitor of		7. 60
			1 22100	monarogramson-z) (COC-ZIIA)	017	36-30
		·	A3/128	metalloproteinase inhibitor 2 precursor	216	3e-56
		:	AAB19474.1	tissue inhibitor of metalloproteinase 2; TIMP-2	216	36-56
	.:		AAĀ59581.1	metalloproteinase inhibitor precursor	. 216	3e-56
		;	AAA61186.1	metalloproteinase-2 inhibitor precursor	216	3e-56
			AAC50729.1	tissue inhibitor of metalloproteinases-2	. 216	3e-56
			1GXD	C Chain C, Prommp-2TIMP-2 Complex	214	1e-55
*:			1GXD	D Chain D, Prommp-2TIMP-2 Complex	214	1e-55
			1BR9 ·	Human Tissue Inhibitor Of Metalloproteinase-2	214	1e-55
·			AAB24785.1	TIMP-2, CSC-21K=tissue inhibitor of metalloproteinase	211	96-55
· .			AAA21815.1	metalloproteinase-3 tissue inhibitor	200	3e-51
			NP_000353.1	tissue inhibitor of metalloproteinase 3; Tissue inhibitor of metalloproteinase-3; K222 expressed in degenerative retinas	199	4e-51
		÷	P35625	TIM3_HUMAN Metalloproteinase inhibitor 3 precursor (TIMP-3) (Tissue inhibitor of metalloproteinases-3) (MIG-5 protein)	f. 199	4e-51
:		·	S45317	metalloproteinase inhibitor 3 precursor	199	4e-51
			AAA17672.1	tissue inhibitor of metalloproteinase-3 precurso	199	4e-51
,• .	. :		CAA53813.1	tissue inhibitor of metalloproteinases-3	199	4e-51
	•		AAB60373.1	tissue inhibitor of metalloproteinases-3	. 199	4e-51
·			AAB34532.1	TIMP-3	. 199	. 4e-51
·			AAC50393.1	tissue inhibitor of metalloproteinases-3	199	4e-51
 	;	·	AAB07547.1	tissue inhibitor of metalloproteinase-3	199	4e-51
			AAH14277.1	AAH14277 Similar to tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory)	. 199	4e-51
•			CAA38400.1	Tissue inhibitor of metalloproteinases, Type-2	199	66-51
NM_008302 NP_032328.1 Mm.2180		Ú(爪D) 2.71	NP 031381.2	heat shock 90kDa protein 1, beta; heat shock 90kD protein 1, beta; Heat-shock 90kD protein-1, beta	. 1202	

			P08238	HS9B_HUMAN Heat shock protein HSP 90-beta (HSP 84) (HSP 90)	1202	C
		,	AAA36026.1	90 kD heat shock protein	1202	0
			AAH04928.1	AAH04928 Unknown (protein for MGC:10493)	1202	C
			AAH12807.1	AAH12807 Unknown (protein for MGC:3483)	1202	C
			AAH14485.1	AAH14485 Unknown (protein for MGC:23206)	1202	0
	ì		AAH16753.1	AAH16753 Unknown (protein for MGC:1138)	1202	°
:		; ;	нини84	heat shock protein 90-beta [validated]	1197	0
			AAA36025.1	90kDa heat shock protein	1197	0
			1307197A	heat shock protein 90k	1197	0
			T46243	hypothetical protein DKFZp761K0511.1	1170	0
	: :		CAB66478.1	hypothetical protein	1170	0
*			NP 005339.1	heat shock 90kDa protein 1, alpha; heat shock 90kD protein 1, alpha	1099	0
			HHHU86 .	heat shock protein 90-alpha	1099	0
			AAA63194.1	heat shock protein	1099	0
	· · ·	; ; ;	AAF82792,1	AF275719 1 chapsions protein HSP90 beta	1052	0
			AAH09206.1	AAH09206 heat shock 90kD protein 1, beta	1052	0
			AAH23006.1	Unknown (protein for MGC:30059)	961	0
	::		AAH00987.1	AAH00987 Unknown (protein for IMAGE:3446372)	800	0
		, ;	AAC25497.1	Hsp89-alpha-delta-N	750	0
			AAH07989.1	AAH07989 Similar to heat shock 90kD protein 1, alpha	969	.0
NM_009056 NP_033082.1 Mm_102	Mm. 102	U:(IR-D) 2.63	NP 602309.1	regulatory factor X2, isoform b; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	. 1166	
	: '		P48378 · · ·	RFX2 HUMAN DNA-binding protein RFX2	1153	
1			B55926	DNA binding protein RFX2	1153	0
``	,		CAA53705.1	DNA binding protein RFX2	1153	0
:			NP 000626.2	regulatory factor X2, isoform a; trans-acting regulatory factor 2; DNA binding protein RFX2; HLA class II regulatory factor RFX2	1152	0

	. :		AAH28579.1	regulatory factor X, 2 (influences HLA class II expression)	1151	6
	;		NP 602304.1	regulatory factor X3 isoform b; DNA binding protein RFX3	7773	
'.		•	AAH22191.1	AAH22191 Unknown (protein for MGC:3664)	773	0
	. ,	1.0	NP 002910.1	regulatory factor X3 isoform a; DNA binding protein RFX3	751	0
			P48380 ·	RFX3_HUMAN DNA-binding protein RFX3	751	0
			D55926	DNA binding protein RFX3.	751	0
	:		CAA53706.1	DNA binding protein RFX3	751	C
			P22670	RFX1_HUMAN MHC class II regulatory factor RFX1 (RFX) (Enhancer factor C) (EF-C)	. 686	0
			A35913	regulatory factor X	989	0
			CAA41730.1	MHC class II regulatory factor RFX	989	0
			NP 002909.2	regulatory factor XI; trans-acting regulatory factor 1; enhancer factor C; MHC class II regulatory factor RFX	989	0
		· '	CAC88163.1	bA32F11.1.2 (regulatory factor X, 3 (influences HLA class II expression), putative isoform 2)	. 507	e-143
			CAC88164.1	bA32F11.1.1 (regulatory factor X, 3 (influences HLA class Ilexpression), isoform 1)	486	e-136
NM_026346 NP_080622.1	Mm.4046 6	U:(IR-D) 2.28	NP_478136.1	F-box only protein 32 isoform 1; muscle atrophy F-box protein; atrogin-1	710	, :
			Q969P5	FX32_HUMAN F-box only protein 32 (Muscle atrophy F-box protein) (MAFbx) (Atrogin-1)	710	0
: .,			AAL16407.1	muscle atrophy F-box protein	710	0
			BAB71333.1	unnamed protein product	710	0
».: \	Y S	÷	CAD12251.1	F-box only 32	710	0
			BAB85128.1	F-box domain Fbx25-containing protein	446	e-124
			NP 680482.1	F-box only protein 32 isoform 2; muscle atrophy F-box protein; atrogin-1	422	e-117
			AAH24030.1	similar to RIKEN cDNA 4833442G10 gene	417	e-116
			AAF04526.1	AF174605 1 F-box protein Fbx25	354	4e-97
			NP 036305:1	F-box only protein 25; F-box protein Fbx25	353	66-97
			:			

	74.7	•				•
 Mm 15	934i L	Mm.19341 U:(IR-D)				
∞	2	.26	AAA51547.1	alpha-1-antitrypsin precursor	508	e-144
· . :	:		AAH15642.1	AAH15642 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antirypsin), member 1	508	e-144
			1012287A	antityypsin alpha1 mutant	507	e-143
! \.			P01009	A1AT_HUMAN Alpha-1-antitrypsin precursor (Alpha-1 protease inhibitor) (Alpha-1-antiproteinase) (PRO0684/PRO2209)	507	. e-143
		٠	ITHU :-	alpha-1-antitypsin precursor [validated]	507	e-143
			CAA25838.1	alpha 1-antitrypsin	507	e-143
	- 1		AAB59375.1	alpha-1-antitrypsin	. 507	e-143
.:			AAG35496.1	AF130117_27 PRO2209	507	e-143
. A.	; :		NP_000286.2	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1; Protease inhibitor (alpha-1-antitrypsin); protease inhibitor 1 (anti-elastase), alpha-1-antitrypsin	506	 e-143
;	:	•	AAH11991.1	AAH11991 Similar to serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase; antitypsin), member 1	506	e-143
•	.		AAF29581.1	AF113676 1 PRO0684	504	e-142
_			AAB59495.1	alpha-1-antitrypsin	504	e-142
			XAA51546.1	alpha-1-antitrypsin	501	e-141
		·	 1HP7 .	Chain A, A 2.1 Angstrom Structure Of An Uncleaved Alpha-1- Antitrypsin Shows Variability Of The Reactive Center And Other Loops	499	e-141
	-		1KCT.	Alpha1-Antitrypsin	498	e-141
NM_009194 NP_033220.1 Mm.4168		U:(R-D) 2.16	NP 001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters),	1978	0
		÷	P55011	S122_HUMAN Solute carrier family 12 member 2 (Bumetanide-sensitive sodium-(potassium)-chloride cotransporter 1) (Basolateral Na-K-Cl symporter)	1978	0
·i	+	: "	A57187	bumetanide-sensitive Na-K-Cl cotransporter	1978	0
			AAC 0561.1.	burnetanide-sensitive Na-K-Cl cotransporter	1978	0
•		•	:			7

1			AAH33003.1	Similar to solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1851	
			NP 000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12 (sodium/potassium/chloride transporters),	1294	0
			 Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitiv sodium-(potassium)-chloride cotransporter 2) (Kidney-specific Na-K-Cl symporter)	1294	0.
·			AAB07364.1	bumetanide-sensitive Na-K-2CI cotransporter	1294	0 ::
: .			NP 000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters)	1028	
	· · · ·	N.		thiazide-sensitive Na-Cl	1028	0
			P55017	S123_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride cotransporter) (Na-Cl symporter)	1024	0
	and the second		G01202	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
			CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	1021	0
			AAL32454.1	AF439152_1 sodium-potassium-chloride cotransporter	598	.e-170
		·,	PC4180	thiazide-sensitive sodium-chloride cotransporter.	413	e-114
			ААН40138.1	Similar to solute carrier family 12 (sodium/potassium/chloride	403	. e-111
			AAK21008.1	cation-chloride cotransporter-interacting protein 1	261	1e-68
NM_009254 NP_033280.1	Mm.2623	U:(IR-D) 2.15	NP 004559.2	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6; protease inhibitor 6 (placental thrombin inhibitor)	549	e-156
	, p		P35237 ::	PTI6_HUMAN Placental thrombin inhibitor (Cytoplasmic antiproteinase) (CAP)(Protease inhibitor 6) (PI-6)	549	e-156
			AAB30320.1	cytoplasmic antiproteinase; CAP	549	. e-156
			AAH01394.1	AAH01394 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6	549	e-156
· · · · · · · · · · · · · · · · · · ·	,	:	A48681	placental thrombin inhibitor	548	e-156
	; *		CAA80373.1	thrombin inhibitor .	548	e-156
		• • • • •	NP 002631.1	scrinc (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 8; protease inhibitor 8 (ovalbumin type)	459	e-129

					•	
	71		P50452	SPB8_HUMAN Cytoplasmic antiproteinase 2 (CAP2) (CAP-2) (Protease inhibitor 8)(Serpin B8)	450	
			A59273	proteinase inhibitor 8	450	6-129
	```		AAC41939.1	cytoplasmic antiproteinase 2	459	6-170
			NP 004146.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9; protease inhibitor 9 (ovalbumin type)	445	e-125
		· .	P50453	SPB9_HUMAN Cytoplasmic antiproteinase 3 (CAP3) (CAP-3) (Protease inhibitor 9)(Serpin B9)	746	201.0
:			B59273	proteinase inhibitor 9	445	P-125
			AAC41940.1	cytoplasmic antiproteinase 3	4	e-125
		• •	AAC50793.1	serine proteinase inhibitor	445	e-125
			AAH02538.1	AAH02538 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9	445	e-125
		:	BAB91078.1	serine protease inhibitor 9	445	e-125
<i>;</i>			NP_109591.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1; protease inhibitor 2 (anti-elastase), monocyte/neutrophil; protease inhibitor 2 (anti-elastase), monocyte/neutrophil derived	330	39.00
	; ;;		P30740	ILEU_HUMAN Leukocyte elastase inhibitor (LEI) (Monocyte/neutrophil elastase inhibitor) (MNEI) (EI)	330	26.00
		: 4	S27383	elastase inhibitor	330	36-90
i.			AAC31394.1.	monocyte/neutrophil elastase inhibitor	330	3e-90
1 11 10 10 10 10 10 10 10 10 10 10 10 10		: :	AAH09015.1	AAH09015 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 1	330	3e-90
W. 7			XP 036951.4	similar to Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
			P48594	SCC2_HUMAN Squamous cell carcinoma antigen 2 (SCCA-2) (Leupin)	327	2e-89
			CAA61420.1	leupin	327	26-89
			ÁAA97553.1	squamous cell carcinoma antigen 2	327	2e-89
			AAA92602.1	squamous cell carcinoma antigen	327	2e-89
				squamous cell carcinoma antigen 2	327	2e-89
			401.1	AAH17401 Unknown (protein for MGC:27150)	327	2e-89
			138202	leupin precursor	327	2e-89

	;; ;		I38201	squamous cell carcinoma antigen 1	325	7e-89
N.	i si Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa Signa S		 NP 008850.1	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 3; squamous	37.5	6
			P29508	SCC1 HUMAN Squamous cell carcinoms antigen 1 (SCCA-1) (Protein TA-A)	325	00 00
			AAA86317.1	squamous cell carcinoma antigen	225	00 80
			AAA97552.1	squamous cell carcinoma antigen 1	325	06-80
			AAH05224.1	AAH05224 serine (or cysteine) proteinase inhibitor, clade B (oyalbumin). member 3	325	96-80
:			AAB20405.1	squamous cell carcinoma antigen; SCC antigen	325	96-89
NM_019431 NP_062304.1	Mm.1037 24	U:(TR-D) 2.09	NP_055220.1	voltage-dependent calcium channel gamma-4 subunit; neuronal voltage-gated calcium channel gamma-4 subunit	54 <u>0</u>	e-153
	: .		Q9UBN1	CCG4_HUMAN Voltage-dependent calcium channel gamma-4 subunit (Neuronal voltage-gated calcium channel gamma-4 subunit)	540	e-153
			AAF03090.1	calcium channel gamma 4 subunit	540	· e-153
	:	·	AAF14538.1	AF162692_1 putative voltage-gated calcium channel gamma-4 subunit	540	e-153
: : ::,			AAH34532.1	calcium channel, voltage-dependent, gamma subunit 4	540	e-153
			NP_006069.1	voltage-dependent calcium channel gamma-2 subunit; stargazin; neuronal voltage-gated calcium channel gamma-2 subunit	303	2e-82
			Q9Y698	CCG2_HUMÁN Voltage-dependent calcium channel gamma-2 subunit (Neuronal voltage-gated calcium channel gamma-2 subunit)	303	2e-82
			AAD22738.1	AF096322_1 neuronal voltage-gated calcium channel gamma-2 subunit	303	26-82
			AAL50049.1	AF361354_1 voltage-dependent calcium channel gamma-8 subunit	302	4e-82
	. :		NP_114101.4	voltage-dependent calcium channel gamma-8 subunit; neuronal voltage-gated calcium channel gamma-8 subunit	300	2e-81
			Q8WXS5	CCG8_HUMAN Voltage-dependent calcium channel gamma-8 subunit (Neuronal voltage-gated calcium channel gamma-8 subunit)	300	2e-81
	•		AAK20031.1	AF288388_1 calcium channel gamma subunit 8	300	2e-81
		. ;	NP_006530.1	voltage-dependent calcium channel gamma-3 subunit; neuronal voltage-gated calcium channel gamma-3 subunit	298	8e-81
; <b>!</b> -	: .'		060359	CCG3_HUMAN Voltage-dependent calcium channel gamma-3 subunit (Neuronal voltage-gated calcium channel gamma-3 subunit)	298	8e-81
•						

·	:	:	AAC152461	Unknown cene product		
			4 4 TOOLOG 1	Trescent .	298	8e-81
			AAD22/39.1	Ar 100346 1 neuronal voltage gated calcium channel gamma-3 subunit	298	8e-81
			AAF42975.1	AF134640 1 calcium channel gamma subunit 3	298	8e-81
			AAH40005.1	calcium channel, voltage-dependent, gamma subunit 3	298	8e-81
		,	XP 050231.1	similar tö calcium channel gamma subunit 8	270	2e-77
· ·	·		AAK15019.1	AF234892 1 putative voltage gated calcium channel gamma-8 subunit CACNG8		
NM_019999 NP_064383.1	Mm.1772 72	U:(IR-D) 2.05	NP_072094.1	KIAA1184 protein	629	0
	. 1		AAH02937.1	AAH02937 Similar to hypothetical protein MNCh-5687	640	
			BAA86498.1	KIAA1184 protein	570	P-165
		\$4. 1.	AAH36457.1	Unknown (protein for MGC:33461)	579	e-165
· ·		,				
		٠				I
AK002297						T
	Mm.18130 U:(C-IR)	U:(C-IR)				
BAB21996.1	2	6.3.	NP 060464.1	hypothetical protein FLJ10099		
	i		BAA91444.1	umamed protein product	620	e-177
	: ::,	: (1)	AAH08675.1	hypothetical protein FL 110099	620	e-177
			AAH12562.1	Similar to hypothetical protein FLJ10099	. 620	e-177
		h	AAH10519.1	Similar to hypothetical protein FLJ10099	. 385	e-106
	;	U:(C-R)	NP_478137.1	zinc finger protein 354B	1031	0.
NM 013744	Mm.7467	U.(IR-D)	•			· .
NP 038772.1	0	2.04			1	
		;	BAB71556.1	unnamied protein product	1031	c
			AAD05335.1	zinc finger protein BZNF	958	C
			NP 005640.1	transcription factor 17	957	6
		•	O60765 ·	TC17 HUMAN Transcription factor 17 (Zinc finger protein eZNF)	957	0

:	; ;		. '			
			BAA25182.1	HKL1.	957	0
***			NP 009080.1	zinc finger protein 184 (Kruppel-like)	267	e-161
	; 		AAH22992.1	Unknown (protein for MGC:29879)	. 567	e-161
	:		AAC51180.1	kruppel-related zinc finger protein	267	e-161
:	į		XP 166367.1	similar to Zinc finger protein 184	995	e-161
	·		099676	Z184_HUMAN Zinc finger protein 184	366	e-161
			CAA17278.1	b34I8.1 (zinc finger protein 184 (Kruppel-like))	566	e-161
			XP 032054.2	similar to BZFIT-related protein 1	536	e-152
			AAK30252.1	AF352026_1 EZFIT-related protein 1	536	e-152
<i>:</i>		•	CAD38551.1	hypothetical protein	. 536	e-152
	·		XP 091988.1	similar to zinc finger protein 91 (HPF7, HTF10)	533	e-151
. :	·: :	·	AAH36110.1	Similar to zinc finger protein 208	531	e-150
NM_018764 NP_061234.1	Mm.1196 4	U:(C-IR) 4.56	NP_002580.2	protocadherin 7, isoform a precursor; BH-pcdh; BH-protocadherin (brain-heart); brain-heart protocadherin	1856	0
: :: '	·		060245	PCH7_HUMAN Protocadherin 7 precursor (Brain-heart protocadherin) (BH-Pcdh)	1855	0
	· . ' ·		BAA25194.1	PCDH7 (BH-Pcdh)a	1855	0
	: · · ·	· • · ·	NP_115832.1	protocadherin 7, isoform b precursor; BH-pcdh; brain-heart protocadherin; BH-protocadherin (brain-heart)	1838	0 .
	!	:	T00041 -	BH-protocadherin PCDH7 (clone BH-Pcdh-b)	1837	0
:			BAA25195.1	PCDH7 (BH-Pcdh)b	1837	0
·	i s f		NP_115833.1	protocadherin 7, isoform c precursor; BH-pcdh; brain-hearl protocadherin; BH-protocadherin (brain-heart)	1691	0 ·.
	· •	7 7 7	T00042 · · · ·	BH-protocadherin PCDH7 (clone BH-Pcdh-c)	1690	0
			BAA25196.1	PCDH7 (BH-Pcdh)c	1690	0
		1 .	NP_115796.1	protocadherin 1, isoform 2 precursor; protocadherin 42; cadherin-like protein 1	817	0
	1.		AAH35812.1	Similar to protocadherin 1 (cadherin-like 1)	816	0
,		3	NP_002578.1	protocadherin 1, isoform 1 precursor; protocadherin 42; cadherin-like protein 1	816	0
			Q08174	PCH1_HUMAN Protocadherin 1 precursor (Protocadherin 42) (PC42) (Cadherin-like protein 1)	816	0
	; ;					

		·	XAA36419.1	protocadherin 42	816	0
			NP_065136.1	protocadherin 9 precursor; cadherin superfamily protein VR4-11	575	e-163
	:	: 	AAF89689.2	AF169692_I protocadherin-9	575	e-163
NM 008121	: : : : : : :	U:(C-IR) 4.51				
NP 032147.1	Mm.19038 6	U:(C-D) 2.06:	NP_005257.2	gap junction protein, alpha 5, 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)	580	e-165
			P36382	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)	280	· e-165
			AAA91833.1	connexin 40	280	e-165
		;;	AAD37801.1	AF151979_1 connexin 40	280	e-165
	* . " . "		AAA60457.2	comexin40	580	e-165
:			AAH13313.1	gap junction protein, alpha 5, 40kD (connexin 40)	580	. · e-165
1		:	I38429 · · · ·	connexin40	575	e-164
	· · · · · · · · · · · · · · · · · · ·		NP_068773.2	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)	301	16-81
:		·	CAC16957.1	bA264J4.3 (novel connexin (gap junction protein)	301	16-81
	· ·		О9У6Н8	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)	301	1e-81
		:	AAD42925.1	gap-junction protein alpha 3	301	. 1e-81
		. :	:. . '.	gap junction protein, alpha 8, 50kDa (comexin 50); gap junction membrane channel		
·. ·	::::	• .	NP 005258.1	(connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)	299	4e-81
	:		139176	intrinsic membrane protein MP70	. 299	4e-81
			AAA77062.1	gap junction membrane channel protein alpha-8	299	4e-81
			P48165	CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)	296	36-80
			AAF32309.1	AF217524_1 gap junction protein alpha 8	296	3e-80
:			AAK55516.1	AF271261_1 comexin 58	282	5e-76
	:		NP_110399.1	connexin 59; gap junction alpha 10	282	5e-76
		·	P57773	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)	282	5e-76
		•				

			AAG09406.1	AF179597_I connexim 59	282	5e-76
			AAD56533.1	AF180815_1 truncated connexin 37 polymorph	270	2e-72
			NP 115991.1	соппехіп 62	797	2e-71
	i .,	· · · · · · · · · · · · · · · · · · ·	AAK51676.1	AF296766_1 connexin 62	267	· · 2e-71
			CAC93847.1	connexin62	267	2e-71
		U:(C-R)				
NM_008314		4:49 [[[(C-D)	· · ·			•
NP_032340.1	Mm:4835	2.43	I37107	5-HT5A serotonin receptor	584	e-166
			CAA57168.1	5-HT5A serotonin receptor	584	e-166
	.; .;	: ::	AAM21132.1	AF498985_1 5-hydroxytryptamine receptor 5A	584	e-166
. ,			BAA94458.1	5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
			NP_000856.1	5-hydroxytryptamine (serotonin) receptor 1E	212	2e-54
			P28566	5H1E_HUMAN 5-hydroxytryptamine 1E receptor (5-HT-1E) (Serotomin receptor)	212	20.54
			A45260	serotonin receptor 1E	212	. 2e-54
			CAA77558.1	serotonin receptor	212	2e-54
			AAA58353.1	serotonin receptor	212	2e-54
	· ;	÷	AAA58355.1	serotonin receptor	212	2e-54
ж. х		·	CAC10582.1	bA76H14.2 (5-hydroxytryptamine (serotonin) receptor 1B)	212	2e-54
: ':	:		AAM21127.1	AF498980_1 5-hydroxytryptamine receptor 1E	212	2e-54
	:	·	NP 000857.1	5-hydroxytryptamine (serotonin) receptor 1F; 5-hydroxytryptamine receptor 1F	209	1e-53
	:		P30939	5H1F_HUMAN 5-hydroxytryptamine 1F receptor (5-HT-1F) (Serotonin receptor)	209	1e-53
·			A47321	serotonin receptor 1F	209	1e-53
	•	,	AAA36605.1	serotonin receptor	209	1e-53
		٠	AAA36646.1	serotonin receptor	209	1e-53
			AAM21128.1	AF498981_1 5-hydroxytryptamine receptor 1F	209	1e-53
			BAA90453.1	5-hydroxytryptamine (serotonin) receptor 1F	209	1e-53

•			,			
		· .	XP_003692.2	similar to 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotonin receptor) (5-HT1A) (G-21)	. 205	1e-52
			P08908	5H1A_HUMAN 5-hydroxytryptamine 1A receptor (5-HT-1A) (Serotonin receptor) (5-HT1A) (G-21)	205	1e-52
	: . !		I38209	serotonin receptor 1A	205	1e-52
	i .		CAA40962.1	serotonin 5-HT1a receptor	205	1e-52
	•:	:	AAA66493.1	serotonin receptor	205	1e-52
	:		BAA94488.1	serotonin receptor 1A	205	1e-52
			AAM21125.1	AF498978_1 5-hydroxytryptamine receptor 1A	205	. 1e-52
\ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\			XP_092299.1	similar to KIAA0622 protein - human (fragment)	205	1e-52
	•••		NP_000854.1	5-hydroxytryptamine (serotonin) receptor 1B; 5-HT1B; 5-HT1DB	204	2e-52
			- P28222	5H1B_HUMAN 5-hydroxytryptamine 1B receptor (5-HT-1B) (Serotonin receptor)(5-HT-1D-beta) (Serotonin 1D beta receptor) (S12)	204	
: : .			JN0268	serotonin receptor 1B	204	2e-52
· · · · · · · · · · · · · · · · · · ·		١.	AAA58675.1	serotonin 1Db receptor	204	2e-52
	;		AAA36029.1	serotonin receptor	204	2e-52
•			AAA36030.1	5-hyroxytryptamine 1D receptor	204	2e-52
			BAA01763.1	serotonin 1B receptor	204	2e-52
	: ,		AAA60316.1	serotonin 1D receptor	204	2e-52
	1.	:	CAB51537.1	dJ501M23.1 (5-hydroxytryptamine (serotonin) receptor 1B)	204	. 2e-52
		 	BAA94455.1	5-hydroxytryptamine (serotonin) receptor 1B	204	2e-52
			2209242B	serotonin receptor:ISOTYPE=1D-beta	204	Że-52
;:			NP_000515.1	5-hydroxytryptamine (serotonin) receptor 1A	202	2e-51
			CAA31908.1	receptor protein (AA 1 - 421)	202	2e-51
			AAA36440.1	guanine nucleotide-binding regulatory protein-coupled recepto	202	· 2e-51
			1311340A.	G protein coupled receptor	202	2e-51
•		•				

						•
NM 009183		U:(C-IR) 4.19				,
	U:(C Mm.10701 2.35	U:(C-D) 2.35	NP_005659.1	sialyltransferase 8D (alpha-2, 8-polysialytransferase); Polysialyltransferase; sialyltransferase 8 (alpha-2, 8-polysialytransferase) D	714	
	: ; . !	ŕ.,	Q92187	SISD_HUMAN CMP-N-acetylneuraminate-poly-alpha-2,8-sialyl transferase (Alpha-2,8-sialyltransferase 8D) (ST8Sia IV) (Polysialyltransferase-1)	714	
		••	I59403	alpha-2,8-polysialyltransferase	714	0
	- princip.		AAC41775.1	alpha-2,8-polysialyltransferase	714	0
		٠	2116443A	polysialyltransferase	714	0
			NP_006002.1	sialyltransferase 8B (alpha-2, 8-sialytransferase); Sialyltransferase X; sialyltransferase 8 (alpha-2, 8-sialytransferase) B	429	e-119
			Q92186	SI8B_HUMAN Alpha-2,8-sialyltransferase 8B (ST8Sia II) (Sialyltransferase X)(STX)	429	e-119
		•	I39169	sialyltransferase	429	e-119
			AAC24458.1	sialyltransferase	429	e-119
·	·		AAB51242.1	sialyltransferase X	429	. e-119
			2123358A·	sialyltransferase STX	429	e-119
	:		B54898	STX protein	330	2e-89
<u>!</u> .			AAA36613.1	sialyltransferase	330	2e-89
	:	:	AAH27866.1	Similar to sialyltransferase 8D (alpha-2, 8-polysialytransferase)	. 320	1e-86
		:	AAC15901.1	alpha-2,8-sialyltransferase III	219	3e-56
	1		NP_056963.1	sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase); alpha-2,8-sialyltransferase III	215	. 8e-55
	1		043173	SI8C_HUMAN Sia-alpha-2,3-Gal-beta-1,4-GlcNAc-R:alpha 2,8-sialyltransferase (Alpha-2,8-sialyltransferase 8C) (ST8Sia III)	215	8e-55
•			AAB87642.1	Sia alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase	. 215	8e-55
NM_009520	: : : :	U:(C-IR) 4.15		wingless-type MMTV integration site family, member 2B, isoform WNT-2B2.		
NP_033546.1	Wm.10740 3.21	U:(C-D) 3.21	NP_078613.1	wingless-type MMTV integration site family, member 13; XWNT2, Xenopus, homolog of	726	
			Q93097	WN2B HUMAN WNT-2B protein precursor (WNT-13)	726	0

	1		DAD110051	11 TO TO TO TO THE PARTY OF THE		
			DAD11903.1	WIN1-425 ISOIOITH 2	726	0
			NP_004176.2	wingless-type MMTV integration site family, member 2B, isoform WNT-2B1; wingless-type MMTV integration site family, member 13; XWNT2, Xenopus, homolog of	702	0
		· ·	BAB11984.1	WNT-2B Isoform.1	702	0
			T09612	secreted glycoprotein Wnt-13	969	0
	i".		CAA96283.1	Wnt-13	969	0
			NP 003382.1	wingless-type MMTV integration site family member 2 precursor; int-1 related protein: oncogene INTI-like 1: secreted growth factor	538	150
			P09544	WNT2_HUMAN WNT-2 protein precursor (IRP protein) (Int-1 related protein)	. 535	e-152
			S00834	int-1-like protein 1 precursor	535	e-152
		• : . :	CAA30725.1	Irp protein (AA 1-360)	535	e-152
			AAH29854.1	wingless-type MMTV integration site family member 2	535	e-152
	· ·	: : i j	AAB67043.1	secreted growth factor	404	e-112
			NP_003383.1	wingless-type MMTV integration site family, member 5A precursor; proto-oncogene Wnt-5A precursor; WNT-5A protein precursor	360	2e-99
:	:		P41221	WN5A_HUMAN WNT-5A protein precursor	360	2e-99
·	::		A48914	proto-oncogene Wnt-5A precursor	360	2e-99
.;	. ;		AAA16842.1	hWNT5A	360	2e-99
	: ;		 NP 116031.1	wingless-type MMTV integration site family, member 5B precursor; WNT-5B protein precursor.	358	1-98
,			NP_110402.2	wingless-type MMTV integration site family, member 5B precursor:	: 358	1e-98
4 			WNT-5B			
:			protein precursor		358	16-08
·		·	Q9H1J7	WNSB_HUMAN WNT-5B protein precursor	358	1e-98
			AAH01749.1	AAH01749 Similar to wingless-related MMTV integration site 5B	358	1e-98
			BAB62039.1	WNT5B	358	1e-98
			NP 478679.1	wingless-type MMTV integration site family, member 7B precursor	355	1e-97

P56706 WN7B HUMAN WNT-7B protein precursor.	355	1e-97
BAB68399.1 WNT7B	355	1e-97
AAH34923.1 wingless-type MMTV integration site family, member 7B	355	1e-97
AAN32640.1 AF416743_1 WNT7B	355	1e-97
wingless-type MMTV integration site family, member 7A precursor; proto-oncogene NP_004616.2 Winf7a protein.	348	1e-95
AAH08811.1 Unknown (protein for MGC:10346)	348	1e-95
AAG38659.1 WNT5b precursor	348	2e-95
U.(C-IR)		
U:(C-D)	-	•
U:(R-D)   CCR4-NOT transcription complex, subunit 2; NOT2 (negative regulator of Mm.22533 2.42   NP 055330.1 transcription 2 veast) homolog		:
AAF29827.1	24.4	٥
	877	0
- AAH11826.1 Similar to CCR4-NOT transcription complex, subunit 2	877	0
BAA91313.1 unnamed protein product	751	0
AAF29095.1 AF161480_1 HSPC131	729	0
AAG39297.1 AF113226_1 MSTP046	728	0
T46494 hypothetical protein DKFZp434M0572.1	326	8e-89
CAB70869.1 hypothetical protein	326	8e-89
U.(C-IR)	: ` `	
U:(C-D) a disintegrin and metalloprotease domain 11, isoform 1 preproprotein;    Mm.89854   2.86   NP_002381.2   metalloproteinase-like, disintegrin-like, cysteine-rich protein	1454	
BAA32352.1 MDC/ADAM11	1454	0
AD11_HUMAN ADAM 11 precursor (A disintegrin and metalloproteinase domain 075078 11) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein) (MDC)	1451	6
165967 disintegrin-like metalloproteinase (BC 3.4.24), splice form 2	1345	0
	0тт 2	orm 2 1345

	:		BAA06670.1	metalloprotease/disintegrin-like protein	1340	0
			NP_067625.1	a disintegrin and metalloprotease domain 11, isoform 2 preproprotein; metalloproteinase-like, disintegrin-like, cysteine-rich protein	101	C
		·	S38539 · ·	disintegrin-like metalloproteinase (BC 3.4.24), splice form 1	. 1011	0 0
,,	÷	:	AAB29191.1	MDC=metalloprotease/disintegrin-like cysteine-rich protein [human, cerebellum, Peptide, 524 aa]	101	· . c
·.			BAA04213.1	MDC protein	101	
			BAA06671.1	metalloprotease/disintegrin-like protein	1008	0
			NP_068367.1	a disintegrin and metalloproteinase domain 22 isoform 5 proprotein; MDC2 delta	825	0
	:	·	BAA32350.1	MDC2 beta	825	0
	. :		AAF22476.2	AF073291_1 MDC2	825	0
: ,		•	NP_057435.2	a disintegrin and metalloproteinase domain 22 isoform 3 proprotein; MDC2 delta	825	
		:	NP_068368.2	a disintegrin and metalloproteinase domain 22 isoform 2 proprotein; MDC2 delta	825	0
AK002979		U:(C-IR) 3.58				
BAB22492.1	Мт.19588 U:(С.D) 1.	U:(C-D) 2.07	NP 056537.1	calcyon		
			Q9NYX4	DIP HUMAN D1 doparnine receptor-interacting protein calcum	336	26-92 5e 02
,			AAF34714.1	AF225903 1 D1 doparmine receptor interacting motein calcuon	336	
			AAH38978.1	Similar to calcyon; D1 dopamine receptor-interacting protein	336	
		U:(C-IR)	:			
NP 032740.1	Mm.31255	5.55 U:(C-D) 2.19	D46531	NTC1_HUMAN Neurogenic locus notch homolog protein 1 precursor (Notch 1)		
			AAG33848.1	AF308602 I NOTCH 1	4040	0 0
	:		A40043.	notch protein homolog TAN-1 precursor	4528	0
	. :		14.1	TAN1	4482	0
			NP_077719.2	notch 2 preproprotein	2628	0
7			AAG37073.1	AF315356 1 NOTCH2 protein	2627	0
•						

	:		Q04721	NTC2_HUMAN Neurogenic locus notch homolog protein 2 precursor (Notch 2) (hN2)	2627	0
		·, ·	AAA36377.2	NOTCH 2	2627	0
.		·	AAC14346.1	Notch3	2065	0
		1.0	NP_000426.1	Notch homolog 3	2065	0
			Q9UM47	NTC3_HUMAN Neurogenic locus notch homolog protein 3 precursor (Notch 3)	2065	0
			S78549 :	notch3 protein	2065	0
			AAB91371.1	Notch3	2065	Ó
	.:		AAC15789.1	Notch 3	2065	0
			NP_004548.1	Notch homolog 4 (Drosophila); Notch, drosophila, homolog of, 4; Notch (Drosophila) homolog 4	1023	0
· (1)	, , ,		099466	NTC4_HUMAN Nemogenic locus notch homolog protein 4 precursor (Notch 4)	1033	
		Ì	AAC32288.1	Notch4	1023	
					1023	0
AK012553	;; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;	U:(C-IR) 3.54				
BAB28313.1	Mm 45628	U:(C-D)	NP: 001575 1	chromosome 11 onen reading frame 0. 22000		
			018777	230E UTMANY Explanation 2000	/70	-i-90
		:	111617	l oram protein 239	627	e-180
			AAC50564.1	239FB gene product	627	e-180
			AAH31582.1	chromosome 11 open reading frame 8	. 627	e-180
		• :	:	239FB gene	627	e-180
			NP 001576.2	chromosome 22 open reading frame 1; 239AB	518	e-147
		•	015442	239A_HUMAN Adult brain protein 239	518	e-147
:			AAC51673.2	239AB	518	: e-147
	•		AAH28035.1	Unknown (protein for MGC:40027)	518	e-147
		,	CAC48257.1	dJ873F21.1 (brain protein 239)	284	2e-76
		,	CAC10467.1	dJ710M3.1 (chromosome 11 open reading frame 8(Fetal brain protein 239))	253	. 5e-67

	_		-			
NM_007412	:	U:(C-IR) 3.52	•			
NP 031438 1	Mm 2857	U:(C-D)	ND 000105 1	adrenomedullin receptor; G-protein-coupled receptor similar to the adrenomedullin		,
1.0CLT CO TAT		0.00	T.C. COO TAIL		563	e-160
,			015218	ADMR_HUMAN Adrenomedullin receptor (AM-R)	563	e-160
:			JC5784	adrenomedullin receptor	563	e-160
			CAA73910.1	G-protein coupled receptor	563	e-160
		÷	AAH34761.1	adrenomedullin receptor	563	e-160
			P25106 -	RDC1_HUMAN G protein-coupled receptor RDC1 homolog -	197	5e-50
	:		A39714	G protein-coupled receptor RDC1	197	5e-50
•	, .	,	AAA62370.1	orphan receptor	197	5e-50
: ,	:		XP_051522.2	similar to G protein-coupled receptor RDC1 homolog	197	5e-50
: : : :			AAH36661.1	Unknown (protein for MGC:33224)	196	6e-50
NM_007488	:.	 -	•			
<u>]</u>		) E				
NP 031514.1	Mm.4813	3.41	Q9HBZ2	ARN2_HUMAN Aryl hydrocarbon receptor nuclear translocator 2 (ARNT protein 2)	1192	0
	2	:	AAG15310.1	AF185610_1 aryl-hydrocarbon receptor nuclear translocator 2	1192	0
			NP_055677.1	aryl-hydrocarbon receptor nuclear translocator 2; KIAA0307 gene product; aryl hydrocarbon receptor nuclear translocator 2	1191	0
- 1	: 1		BAA20766.1	KIAA0307	1191	0
			AAH36099.1	Unknown (protein for MGC:33872)	1165	0
			NP_001659.1	aryl hydrocarbon receptor nuclear translocator	728	0
		*. * . * . * 	P27540	ARNT_HUMAN Aryl hydrocarbon receptor nuclear translocator (ARNT protein) (Dioxin receptor, nuclear translocator) (Hypoxia-inducible factor 1 beta) (HIF-1 beta)	728	0
.s. .: .:		•.	159550	aryl hydrocarbon receptor nuclear translocator Amt [imported]	728	0
	`\	•	AAA51777.1	Arint	728	0
× 1			CAC21446.1	aryl hydrocarbon receptor nuclear translocator, ARNT	728	0
	:		CAD38953.1	hypothetical protein	714	0
		1	AAC03365.1	aryl hydrocarbon receptor nuclear translocator; Arnt	412	e-115

				·	
. :		000327	BMAL_HUMAN BMAL1 protein (Brain and muscle ARNT-like 1) (Member of PAS protein 3) (Basic-helix-loop-helix-PAS orphan MOP3) (BHLH-PAS protein JAP3)	301	2e-81
:		BAA19968.1	BMAL1a	301	2e-81
i		NP_001169.2	aryl hydrocarbon receptor nuclear translocator-like	301	· .2e-81
-		AAB37248.1	bHLH-PAS protein JAP3	301	2e-81
		AAC24353.1	basic-helix-loop-helix-PAS orphan MOP3	301	2e-81
		AAC51213.1	PAS protein 3	. 301	3e-81
	3.3.4	JC5405	brain and muscle Ah receptor nuclear translocator-like protein, BMAL1b	300	5e-81
	;	BAA19935.1	BMAL1b	300	5e-81
;	U.(C-IR)			."	
٥٤٤٥	3.26				
C00%	2.41	NP_005724.1	RAB6 interacting, kinesin-like (rabkinesin6)	1345	0
. :		095235	RB6K_HUMAN Rabkinesin-6 (RAB6-interacting kinesin-like protein) (GG10_2)	1345	0
÷		AAC83230.1	rabkinesin6	1345	0
	. :	AAD37806.1	AF153329_1 RAB6KIFL	1345	0
		AAH12999.1	AAH12999 Similar to RAB6 interacting, kinesin-like (rabkinesin 6)	1345	0
:.		NP_057279.1	M-phase phosphoprotein 1; mitotic kinesin-like protein	333	9e-91
	. ;	T17272 · · ·	hypothetical protein DKFZp434B0435.1	. 333	.9e-91
		CAB55962.1	hypothetical protein	333	96-91
		BAB69456.1	mitotic kinesin-related protein	326	1e-88
	•	NP_004847.2	kinesin-like 5 isoform 2; mitotic kinesin-like 1	201	4e-51
,		Q02241 :	KNS5_HUMAN Mitotic kinesin-like protein-1 (Kinesin-like protein 5)	201	4e-51
		CAA47628.2	mitotic kinase-like protein-1	201	4e-51
	·	NP_612565.1	kinesin-like 5 isoform 1; mitotic kinesin-like 1	201	4e-51
		AAH17705.1	AAH17705 kinesin-like 5 (mitotic kinesin-like protein 1)	201	4e-51
	•	•			٦.

0.57700 NAV		U:(C-IR)				
OCT TOO TATE	•	J.(C-D)			·	· · · · · · · · · · · · · · · · · · ·
NP_031756.1	Mm.3819	$\neg$	NP_004361.2;	alpha 1 type XII collagen, long isoform precursor	5003	
			Q99715	CA1C_HUMAN Collagen alpha 1(XII) chain precursor	4987	0
			AAC51244.1	collagen type XII alpha-1	4987	0
:			NP_542376.1	alpha 1 type XII collagen, short isoform precursor	2961	0
			CAB71222.1	dI238D15.1 (collagen, type XII, alpha 1)	2769	0
· .		,	CAB65984.1	d7234P15.1 (collagen, type XII, alpha 1)	1046	0
		Y .:	AAC01506.1	type XII collagen	. 893	0
			A40970	undulin 1	518	e-146
			AAA36794.1	undulin 1.	518	e-146
		,	CAA72402:1	collagen type XIV	497	e-139
	· .		CAC19497.1	bA209D8.1 (collagen type XII, alpha 1)	464	e-129
***			ÁAH14640.1	Unknown (protein for MGC:15451)	461	e-129
::		Ę,	A35175	mucin 1 precursor, repetitive splice form A [validated]	370	e-102
NM_013605 NP_038633.1	Mm.1619 3	3.1/ U:(C-D) 3.4			•	
			NP_002447.2	mucin 1, transmembrane; peanut-reactive urinary mucin; episialin; polymorphic epithelial mucin; epithelial membrane antigen; DF3 antigen; H23 antigen	368	e-101
	i ; : : : :		P15941	MUC1_HUMAN Mucin 1 precursor (MUC-1) (Polymorphic epithelial mucin) (PEM)	368	· · e-101
			i , }.	(Tumor-associated epithelial membrane antigen) (EMA) (H23AG) (Peanut-reactive urinary mucin) (PUM) (Breast carcinoma-associated antigen DF3) (CD227 antigen)	•	· ·
			AAA60019.1	mucin	368	e-101
	·		CAA36478.1	precursor polypeptide (AA -21 to 494)	325	2e-88
		; , ; ,	AAA59876.1	polymorphic epithelial mucin	317	. 4e-86
		 	AAB53150.1	polymorphic epithelial mucin	317	4e-86
			XP 053256.8	similar to polymorphic epithelial mucin	317	4e-86

			,			
		•	AAA35805.1	episialin variant A precursor	298	2e-80
:	T. *:		AAA35807.1	episialin variant B precursor	298	2e-80
		. :	AAD10858.1	MUC-1/Z mucin short variant	274	5e-73
		÷	S48146	mucin 1 precursor, non-repetitive splice form Y [validated]	272	· ·1e-72
,	·	·	CAA56734.1	MUCI	272	1e-72
		•	AAD10857.1	MUC-1/Y mucin short variant	. 272	1e-72
			AAD27842.1	AF125525_1 MUC1/Y mucin precursor	271	3e-72
	• .		AAD10856.1	MUC-1/X mucin short variant	214	4e-56
NM 008652		U:(C-IR) 3.11	: :			
NP_032678.1		U:(C-D) 2	NP_002457.1	v-myb myeloblastosis viral oncogene homolog (avian)-like 2; B-MYB; v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	, 0
			P10244	MYBB_HUMAN Myb-related protein B (B-Myb)	1123	0
		·	166108	transforming protein B-myb	1123	0
			CAA31655.1	B-myb protein (AA 1-700)	1123	0
			CAC08392.1	dJ1028D15.3 (v-myb avian myeloblastosis viral oncogene homolog-like 2)	1123	0
: 1	. :		AAH07585.1	v-myb avian myeloblastosis viral oncogene homolog-like 2	1123	0 .
			P10243	MYBA_HUMAN Myb-related protein A (A-Myb)	280	1e-74
			S03423	transforming protein A-myb	. 280	.1e-74
·	:		CAA31656.1	A-myb N-terminal region )2341 is 2nd base in codon)	280	1e-74
	1	;	AAB49038.1	alternatively spliced product using exon 9A	276	. 1e-73
-1	· ·	·	CAA36371.1	MYB protein (AA 1-637)	276	1e-73
				v-myb myeloblastosis viral oncogene homolog (avian); v-myb avian myeloblastosis viral oncogene homolog; Avian myeloblastosis viral (v-myb) oncogene homolog:		
			NP 005366.1	c-myb	276	1e-73
		· · · · · · · · · · · · · · · · · · ·	AAA52032.1	c-myb	276	1e-73
			XP_004256.3	similar to Myb proto-oncogene protein (C-myb)	276	1e-73
	1 3		P10242	MYB_HUMAN Myb proto-oncogene protein (C-myb)	276	1e-73
			AAB49039.1	c-myb gene product	276	1e-73

			AAC96326.1	MVB profo-oncovene protein	276	16-73
			TVHUMB	0	276	1e-73
		1	AAB49035.1.	alternatively spliced product using exon 9B	276	1e-73
	;, ;		AAB49036,1	alternatively spliced product using exon 8A	276	1e-73
		U:(C-IR)	:			
	•	2.99				
NTA 000160		U(C-D)				·.
INIMI: UUSIOS		U.(TR-D)		GLK5 HUMAN Glutamate receptor, ionotropic kainate 5 precursor (Glutamate		:
NP_032194.1	Mm.2879	2.41	Q16478	receptor KA-2) (KA2) (Excitatory amino acid receptor 2) (EAA2)	1757	0
· ·		:	157936	glutamate receptor subunit	1757	0
			AAB22591.1	glutamate receptor subunit; EAA2; excitatory amino acid receptor 2	1757	0
			NP_002079.2	glutamate receptor, ionotropic, kainate 5	1625	0
			CAC80547.1	kainate receptor subunit KA2a	1625	0
		:	NP_055434.1	glutamate receptor, ionotropic, kainate 4; excitatory amino acid receptor 1	1254	0
<i>:</i>		· :	016099	GLK4_HUMAN Glutamate receptor, ionotropic kainate 4 precursor (Glutamate receptor KA-1) (KA1) (Excitatory amino acid receptor 1)(EAA1)	.1254	
			JH0826	glutamate ionotropic receptor EAA1 chain precursor	1254	Q.
	٠	•	AĀB29311.1	excitatory amino acid receptor 1; kainate receptor subunit EAA1	1254	0
:.			A54260	glutamate receptor 6 kainate-preferring precursor	704	0
			AAB31362.1	GluR6 kainate receptor—ionotropic-type glutamate receptor	704	0 .
	, ,		NP_068775.1	glutamate receptor, ionotropic, kainate 2	704	0
		·	Q13002	GLK2_HUMAN Glutamate receptor, ionotropic kainate 2 precursor (Glutamate receptor 6) (GluR-6) (GluR6) (Excitatory amino acid receptor 4) (EAA4)	704	
: : ,			AAC50420.1	EAA4	704	0
	١		CAC67487.1	GluR6 kainate receptor	689	0
			CAC81020.1	kainate receptor subunit	289	0
	: 1		Q13003 -	GLK3_HUMAN Glutamate receptor, ionotropic kainate 3 precursor (Glutamate receptor 7) (GluR-7) (GluR7) (Excitatory amino acid receptor 5) (EAA5)	289	0
			NP 000822.1	glutamate receptor, ionotropic, kainate 3	687	0
-						

			AAB60407.1	EAA5	. 687	0
,	- :		AAA95961.1	ВААЗ	685	0
NM 007765	\. \.	U:(C-IR) 2.93	٠.			
	U:(C-D) Mm.22695 2.6	U.(C-D) 2.6	NP_001304.1	collapsin response mediator protein 1; collapsin response mediator protein 1 (dihydropyrimidinase-like 1)	.1036	0
:'	1.		Q14194	DPY1_HUMAN Dihydropyrimidinase related protein-1 (DRP-1) (Collapsin response mediator protein 1) (CRMP-1)	1036	0
			JC5316	dihydropyrimidinase related protein 1	1036	0
•			BAA11190.1	dibydropyrimidinase related protein-1	1036	0.
			AAH00252.1	collapsin response mediator protein 1	1036	0
			AAH07613.i	collapsin response mediator protein 1	1036	0
			AAK55500.1	collapsin response mediator protein 1	963	0 .
			AAA93201.1	hCRMP-1	919	0
			NP_001377.1	dihydropyrimidinase-like 2; collapsin response mediator protein hCRMP-2	847	0 · · ·
**************************************			016555	DPY2_HUMAN Dihydropyrimidinase related protein-2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3)	847	0 :
			JC5317	dihydropyrimidinase-related protein 2	847	0
			AAA93202.1	hCRMP-2	847	0
	) - agri		BAA11191.1	dihydropyrimidinase related protein-2	847	0
			AAC05793.1	N2A3	847	0
			BAA86991.1	dihydropyrimidinase related protein 2	847	0
			NP 001378.1	dihydropyrimidinase-like 3	813	.0
			014195	DPY3_HUMAN Dihydropyrimidinase related protein-3 (DRP-3) (Unc-33-like phosphoprotein) (ULIP protein) (Collapsin response mediator protein 4) (CRMP-4)	813	0
			JC5318	dihydropyrimidinase related protein 3	813	0
			BAA11192.1	dihydropyrimidinase related protein-3	813	0
		÷	AAH39006.1	dihÿdropyrimidinase-like 3	813	0
			CAA69153.1	ULP	810	0.

	·	•	NP_006417.1	dihydropyrimidinase-like 4	. 781	0
			014531	DPY4_HUMAN Dibydropyrimidinase related protein-4 (DRP-4) (ULIP4 protein)	781	0
•	:		BAA21886,1	dihydropyrimidinase related protein 4	781	0
\s\f		•	CAA71872.1	cytosolic phosphoprotein	749	0
			AAH07898.1	Similar to collapsin response mediator protein 1	712	0
NW 009872		U:(C-IR)	: :			
NP 034002.1	Mm.15383 U.(C-D)	7.% U:(C-D) 2.61	NP 003927.1	cyclin-dependent kinase 5, regulatory subunit 2; cyclin-dependent kinase 5 activator isoform p39i: NEURONAL CDK5 activator isoform	. 483	
			1	CD5S HUMAN Cyclin-dependent kinase 5 activator 2 precursor (CDK5 activator 2)	3 .	3
*:			Q13319	(Cyclin-dependent kinase 5 regulatory subunit 2) (P39)(P39I)	483	e-136
			I39172 : .	cyclin-dependent kinase 5 activator isoform p39i	483	e-136
·			AAC50278.1	cyclin-dependent kinase 5 activator isoform p39i	483	e-136
•			2202258:A	cyclin-dependent kinase 5	483	e-136
	: ·		NP_003876.1	cyclin-dependent kinase 5, regulatory subunit 1; regulatory partner for cdk5 kinase; TPKII regulatory subunit	228	1e-59
· ·.				CD5R_HUMAN Cyclin-dependent kinase 5 activator 1 precursor (CDK5 activator 1) (Cyclin-dependent kinase 5 regulatory subunit 1) (Tau protein kinase II 23 kDa	·	
			Q15078	subunit) (TPKII regulatory subunit) (P23) (P25) (P35)	228	1e-59
·			S50861	cyclin-dependent kmase 5 regulatory chain p35	228	1e-59
			CAA56587.1	regulatory partner for cdk5 kinase	228	1e-59
1:	,		AAH20580.1	AAH20580 cyclin-dependent kinase 5, regulatory subunit 1 (p35)	228	1e-59
			2019431A	cyclin-dependent kinase 5:SUBUNIT=p35	228	. 1e-59
	Ì.	: .	AAH26347.1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)	226	4e-59
			AAH30792.1	cyclin-dependent kinase 5, regulatory subunit 1 (p35)	226	4e-59
	•		1H4L	D Chain D, Structure And Regulation Of The Cdk5-P25(Nck5a) Complex	217	2e-56
	i,		1H4L	E Chain E, Structure And Regulation Of The CdtG-P25(Nck5a) Complex	217	. 2e-56
•			:			

					•	
	:	U:(C-IR)	U.(C-IR) XP_093388.1	similar to DnaJ homolog subfamily B member 8 (mDJ6)	336	4e-92
NM 019964 NP 064348.1	Mm.2039 U.(C-D)	2.84 U.(C-D) 3.13				•
· ·	, ,		NP_699161.1	hypothetical protein MGC33884	336	4e-92
			AAH29521.1	Similar to DuaJ (Hsp40) homolog, subfamily B, member 8	336	4e-92
			NP_005485.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform b; Heat shock protein J2	258	7e-69
. ·	•	· .	BAA32209.1	MRJ	258	7e-69
		·	AAD43194.1	AF075601_1 heat shock J2 protein	258	7e-69
	•		AAF21257.1	AF060703_1 DNAj homolog	258	7e-69
	i .		BAA88770.1	DnaJ homolog	258	.7e-69
	: '!*.	;; ;; ;;	CAB66642.1	hypothetical protein	258	7e-69
			AAH00177.1	AAH00177 Similar to DnaJ (Hsp40) homolog, subfamily B, member 6	258	7e-69
	, , ,		XP_052862.4	similar to DnaJ homolog	256	3e-68
: :			NP 490647.1	DnaJ (Hsp40) homolog, subfamily B, member 6 isoform a; Heat shock protein J2	249	99-99
		. : : : : : : : : : : : : : : : : : : :	075190	DJB6_HUMAN DnaJ homolog subfamily B member 6 (Heat shock protein J2) (HSJ-2) (MSJ-1) (HHDJ1) (MRJ)	249	99-99
:		i	BAA88769.1	DnaJ homolog	249	99-99 ·
			AAH02446.1	AAH02446 MRJ gene for a member of the DNAJ protein family	249	99-99
NM 008417	· :	U:(C-IR) 2.82				
D:(C NP_032443.1 Mm.56930 2.47	Mm.56930	U:(C-D)_ 2.47	NP_004965.1	potassium voltage-gated channel, shaker-related subfamily, member 2; voltage-gated potassium channel protein Kv1.2; potassium channel	880	. 0
·			P16389	CIK2_HUMAN Potassium voltage-gated channel subfamily A member 2 (Potassium channel Kv1.2) (RBK2) (HBK5) (NGK1) (MK2) (HUKIV)	880	
:			177466	potassium channel	880	0
			AAA36141.1	potassium channel	988	0 .
	: : : : : : : : : : : : : : : : : : : :		NP_000208.1	potassium voltage-gated channel, shaker-related subfamily, member 1	662	0 .
: , . : , .		· ·	Q09470	CIK1_HUMAN Potassium voltage-gated chamel subfamily A member 1 (Potassium chamel Kv1.1) (HUK1) (HBK1)	662	0

-			157680	potassium channel KCNA1	662	0
			AAA36139.1	potassium channel	662	0
			NP_002223.2	potassium voltage-gated channel, shaker-related subfamily, member 3; potassium channel protein; voltage-gated potassium channel protein Kv1.3; type n potassium channel	009	e-171
}.	٠,		P22001	CIK3_HUMAN Potassium voltage-gated chamel subfamily A member 3 (Potassium chamel Kv1.3) (HPCN3) (HGK5) (HUKIII) (HLK3)	009	e-171
			AAB88073.1	voltage-gated potassium channel	009	e-171
	V	::	AAH35059.1	potassium voltage-gated channel, shaker-related subfamily, member 3	009 .	.e-171
	:		A38101' · ·	potassium chamel KCNA3	599	e-171
. :		;	AAA59457.1	potassium channel protein	. 599	e-171
1 :			AAC31761.1	potassium chamel	298	e-171
:::::::::::::::::::::::::::::::::::::::			AAA36425.1	potassium channel protein	595	e-170
			NP_002224.1	potassium voltage-gated channel, shaker-related subfamily, member 4; potassium voltage-gated channel, shaker-related subfamily, member 4-like; potassium channel KCNA4; shaker-related potassium channel Kv1.4; voltage-gated potassium channel; potassium channel protein; type A potassium channel, rapidly inactivating potassium channel; fetal skeletal muscle potassium channel; cardiac potassium channel; potassium channel 2; voltage-gated potassium channel protein Kv1.4	543	e-154
			A39922 · ·	potassium channel KCNA4	543	e-154
			ÅAA36140.1	potassium channel	543	. e-154
			AAA61275.1	voltage-gated potassium channel	543	e-154
			P22459	CIK4_HUMAN Potassium voltage-gated channel subfamily A member 4 (Potassium channel Kv1.4) (HK1) (HPCN2) (HBK4) (HUKII)	. 541	. e-153
		\	AAA60034.1	potassium channel protein	541	e-153
			NP_002226.1	potassium voltage-gated channel, shaker-related subfamily, member 6; voltage-gated potassium channel-2	519	e-147
	1 :		P17658	CIK6_HUMAN Potassium voltage-gated channel subfamily A member 6 (Potassium channel Kv1.6) (HBK2)	519	e-147
			CAA35623.1	put. HBK2 protein (AA 1-529)	519	e-147
			S12787	potassium channel KCNA2	517	e-146
٠,	٠.	:	1			

	; ; ; ;	U:(C:R)	U.(C-IR) NP_000757.2	cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 13	563	e-160
		2.79				:
NM_013809 NP_038837.1	Mm.1023 12	U:(C-D) 2.22				
		:	AAG35775.1	cytochrome P450 2A13	563	e-160
:	. ;		Q16696	CPAD_HUMAN Cytochrome P450 2A13 (CYPIIA13)	558	
			AAB40519.1	cytochrome P450	558	<u>:</u>
		·	04HUA6. :	coumarin 7-hydroxylase (BC 1.14.14) cytochrome P450 2A6	555	e-158
		:	AAA52067.1	cytochrome P450IIA3	555	e-158
. :	· ;		NP_000753.2	cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 6; coumarin	553	e-157
				7-nydroxyrase; cytocmome F450, subtamily ILA (phenobarbital-inducible), polypeptide 3; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	;	
	; ;	·	P11509	CPA6_HUMAN Cytochrome P450 2A6 (CYPIIA6) (Coumarin 7-hydroxylase) (IIA3) (CYP2A3) (P450(I))	552	e-157
			CAA32118.1	P-450 IIA4 protein (AA 1-494)	552	e-157
_			AAF13600.1	AF182275_1 cytochrome P450-2A6	551	. e-157
			1609083A	cytochrome P450IIA	551	e-156
			CAA32097.1	cytochrome P-450IIA (AA 1 - 489)	551	e-156
	:		P20853	CPA7_HUMAN Cytochrome P450 2A7 (CYPIIA7) (P450-IIA4)	543	e-154
			AAA52138.1	cytochronie P450IIA4	543	e-154
; ,			C34271	cytochrome P450 2A4	543	e-154
	•	U:(C-IR)	NP_003890.1	Rho guamine nucleotide exchange factor 7 isoform a; SH3 domain-containing	1135	0
NM_017402 NP_059098.1	•	U.(C-D) 2.8	. ,	prome-tien protein, r.A.cinteracing exchange factor bera		
	1		Q14155	PIXB_HUMAN Rho guanine nucleotide exchange factor 7 (PAK-interacting exchange factor beta) (Beta-Pix) (COOL-1) (p85)	1135	0
	·	; :	BAA09763.1	The KIAA0142 gene is related to human KIAA0006 gene.	1135	0
:			CAD38906.1	hypothetical protein	1014	0
29			NP_663788.1	Rho guanine nucleotide exchange factor 7 isoform b; SH3 domain-containing proline-rich protein; PAK-interacting exchange factor beta	1014	0
						-

			BAA04985 1	this semience overlans D13631 it covers 054 4350 of this semience	751	C
		:	XP_042963.2	similar to Rho guanine nucleotide exchange factor 6 (PAK-interacting exchange factor		0
		;	NP_004831.1	Rac/Cdc42 guanine nucleotide exchange factor 6; PAK-interacting exchange factor, alpha; Rac/Cdc42 guanine exchange factor (GEF) 6; rho guanine nucleotide exchange factor 6	751	0
			Q15052	ARH6_HUMAN Rho guainine nucleotide exchange factor 6 (PAK-interacting exchange factor alpha) (Alpha-Pix) (COOL-2)	751	0
-			AAH39856.1	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	751	0
1			BAA02796.1	KIAA0006	504	e-142
			1BY1	A Chain A, Dbl Homology Domain From Beta-Pix	385	e-106
•		:	AAH33768.1	Similar to Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	301	4e-81
NM 009819	. ,	U:(C-IR) 2.7				
_ NP_033949.1	Mm.34637	U:(C-D) 2.71	NP_004380.1	catenin (cadherin-associated protein), alpha 2; Catenin, alpha-2(cadherin-associated protein, related)	1684	0
•			P26232	CTN2_HUMAN Alpha-2 catenin (Alpha-catenin related protein) (Alpha N-catenin)	1684	0
			A:AA58407.2	cadherin-associated protein-related	1684	0
			A45011	alpha-catenin 2	1317	0
:	:		XP_038221.1	similar to Alpha-1 catenin (Cadherin-associated protein) (AlphaE-catenin)	1317	0
			P35221 · · ·	CTN1_HUMAN Alpha-1 catenin (Cadherin-associated protein) (Alpha E-catenin)	1317	0 .
	!		N0607	alpha-catenin 1.	. 1317.	0
	`	·	BAA02979.1	alpha-catenin	1317	0
	·	:	AAC99459.1	alphaB-catenin	.1317	0
		:	AAH00385.1	Unknown (protein for MGC:8429)	1317	0
.· .;		·	BAA03530.1	'furnan alpha-catenin'	1313	0
	1 1 2		2023176A	alpha catenin	· 1313	0
	:	:	JC2542	alpha-2(B)-catenin	1290	0
			AAA18949.1	alpha2(B)-catenin	1290	0
						,

	1286 0	1286 0	974 0	974. 0	841 0	389 e-107	389 e-107	380 e-105	3799 0	330 6628	3799 0	3797 0	0 8692	26980	0 . 984	0 984	486 e-136	257 . 2e-67	257 2e-67	257 2e-67		
catenin (cadherin-associated motein) alnha 1 102kDa: catenin (cadherin associated		L ₋	alpha-catenin-like protein	AF091606_1 alphaT-catenin	Similar to catenin (cadherin-associated protein), alpha 2	A Chain A, Alpha-Catenin M-Domain	B Chain B, Alpha-Catenin M-Domain	similar to alpha(E)-catenin	human immunodeficiency virus type I enhancer binding protein 2; human immunodeficiency virus type I enhancer-binding protein 2	· :	MBP-2 (MHC Binding Protein-2)	pe I enhancer-binding protein 2	ZEPZ HUMAN HUMAN IMMUNODEFICIENCY VIRUS TYPE I ENHÄNCER-BINDING PROTEIN 2 (HIV-EPZ)	HIV-EP2/Schnurri-2	human immunodeficiency virus type I enhancer-binding protein 3	AF278765_1 kappa B and V(D)J recombination signal sequences binding protein	KIAA1555 protein	human immunodeficiency virus type I enhancer binding protein 1; human immunodeficiency virus type I enhancer-binding protein 1	ZEP1_HUMAN Zinc finger protein 40 (Human immunodeficiency virus type I enhancer-binding protein 1) (HIV-EP1) (Major histocompatibility complex binding protein 1) (MBP-1) (Pocitive remitters domein II binding to the protein 1) (MBP-1) (Pocitive remitters)	DNA-binding protein PRDII-BF1	PRDII-BF1 protein (AA 1-2717)	DNA-binding protein
	NP_001894.1	AAA86430.1	NP_037398.1	AAF21801.1	AAH31262.1	1H6G	1H6G	XP_068797.2	NP_006725.2	WMHUE2	CAA46596.1	AAF81365.1	P31629	AAB88218.1	NP_078779.1	AAK01082.1	BAB13381.1	NP_002105.1	P15822	A34203	CAA35798.1	AAA17534.1
		,	•	·	·		23-44 · · ·		U:(C-R) 2.68								:		:			
	,								Mm.4215				,		**		: : :		· · ·	1',		
									NM_010437 NP_034567.1													

AK003722	:	U:(C-IR) 2.62.				
BAB22959.1	U:(C Mm.89830 2.18	Â.	NP_008950.1	ubiquitin-conjugating enzyme E2C; ubiquitin carrier protein E2-C	343	2e-94
	·, ·		000762	UBCC_HUMAN Ubiquitin-conjugating enzyme E2 C (Ubiquitin-protein ligase C) (UbcH10)	343	. 2e-94
			AAB53362.1	cyclin-selective ubiquitin carrier protein	343	2e-94
1.			CAB66118.1	ubiquitin-conjugating enzyme E2 H10 (isoform 1)	343	2e-94
			AAH07656.1	ubiquitin carrier protein E2-C	343	, 2e-94
		:	AAH16292.1	ubiquitin-conjugating enzyme E2C	343	2e-94
NM_007511	:	·				
NP 031537.1	U:(C Mm.87854 2.62	U:(C-IR) 2.62	AAB52902.1	AAB52902.1	2285	
:			NP000044.1	ATPase, Cu++ transporting, beta polypeptide (Wilson disease); ATPase, Cu++ transporting, beta polypeptide	. 2282	0
		, , , , , , , , , , , , , , , , , , ,	P35670	AT7B_HUMAN Copper-transporting ATPase 2 (Copper pump 2) (Wilson disease-associated protein)	2282	0
	. 1.		S78555	copper-transporting ATPase (EC 3.6.1) beta	2282	0
,	· ;		AAA92667.1	copper transporting ATPase	2282	0
	1.2	· ·i	2001422A	Cu transporting ATPase P	2149	0
			S40525	copper-transporting ATPase (BC 3.6.1) beta chain	2149	0 .
			004656	AT7A_HUMAN Copper-transporting ATPase 1 (Copper pump 1) (Menkes disease-associated protein)	1484	Ċ
			S36149	copper-transporting ATPase (EC 3.6.1) alpha chain	1484	
		: A	CAB94714.1	Menkes disease	1484	0
			NP_000043.1	ATPase, Cu++ transporting, alpha polypeptide	1484	0
			AAA35580.1	Cu++-transporting P-type ATPase	1484	0
				Menkes disease gene	1467	0
		i .	CAB08162.2-	Menkes Disease (ATP7A)	1420	0
		: :	AAA79212.1	ORF	1022	

UU:	5/08	32398							1	25								rc	1/(	152003	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	3370		
	e-173		· e-120	e-120	: e-120	e-120	e-120	e-120	e-120	e-120's	¢-114	:				e-113	e-113	e-113	,	5e-64	1e-63	1e-63	1e-63	1e-63
	809		431	431	431	431	431	431	431	431	411					409	409	409		241	240	240	240	240
	Wilson disease-associated protein		interleukin 13 receptor, alpha 2 precursor; interleukin 13 binding protein; interleukin 13 receptor alpha 2 chain; IL-13 receptor	I132_HUMAN Interleukin-13 receptor alpha-2 chain precursor (Interleukin-13 binding protein)	interleukin 13 receptor	interleukin-13 receptor	U-13 receptor	dA204F4.1 (interleukin 13 receptor, alpha 2)	interleukin 13 receptor, alpha 2	interleukin 13 receptor, alpha 2	AF089087 1 G protein-coupled receptor					G protein-coupled receptor 35	GP35_HUMAN Probable G protein-coupled receptor GPR35	G protein-coupled receptor		mammary-derived growth inhibitor	fatty acid binding protein 3	similar to Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	FABH_HUMAN Fatty acid-binding protein, heart (H-FABP) (Muscle fatty acid-binding protein) (M-FABP) (Mammary-derived growth inhibitor) (MDGI)	fatty acid-binding protein, cardiac and skeletal muscle - human
	AAA16173.1	• :	NP_000631.1	Q14627	CAA64617.1	AAB17170.1	CAA70021.1	CAD18962.1	AAH20739.1	AAH33705.1	AAG17965.1	. ,	;	-		NP_005292.1	- 09нс97	AAC52028.1	· ;	CAA71305.1	NP_004093.1	XP_049316.1	P05413	FZHUC
		U:(C-IR) 2.61	U:(C-D) 2.38		. : 						U:(C-IR)	2.59	(C-D)	3.35 U:(IR-D)	2.3		i			U:(C-IR) 2.54			, ·.	
		.1.	Mm.20855				; •				; ;; ;;			Mm.1527	80 -	:				Mm.2222 0			:	: A
		NM 008356	NP_032382,1					:		. A		:			NF 0/1/15.1				::	NM_010174 NP_034304.1	• 1.			

Г	240 · 1e-63	240 16-63	240 1e-63	eart (mammary-derived growth 240 1e-63	Acid Binding Protein 238 6e-63	With One Molecule 238 6e-63	h One Molecule 238 6e-63	238	238 6-63	. 237 1e-62	214 9e-56		1206 0	1205 0	1205 0	1197 0	1197. 0	1197 0	209 2e-54			209 ·· 2e-54
Г	240	240	240					•	238	. 237	214		1206	1205	1205	1197	1197	1197	209			209
Г		·		eart (mammary-derived growth	Acid Binding Protein	With One Molecule	h One Molecule	e Molecule											1			
	muscle fatty-acid-binding protein (FABP)	fatty acid binding protein FABP	fatty acid binding protein	AAH07021 fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	A Chain A, Solution Structure Of Human Heart-Type Fatty Acid Binding Protein	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Elaidic Acid	Fatty Acid Binding Protein (Human Muscle, M-Fabp) Complexed With One Molecule Of Blaidic Acid	Fatty Acid Binding Protein (Holo Form, Human Muscle) (M-Fabp)	fatty acid-binding protein	heart fatty acid binding protein; hFABP		cyclin F	CG2F_HUMAN G2/mitotic-specific cyclin F	cyclin F	cyclin F; G2/mitotic-specific cyclin F; F-box only protein 1	cyclin F	cyclin F [Homo sapiens]	lymphocyte antigen 6 complex, locus H			LY6H_HUMAN Lymphocyte antigen Ly-6H precursor
	CAA39889.1	AAB02555.1	AAC99800.1	AAH07021.1	1G5W	1 HIMR	1HIMS	1HMT	2HIMB	1714345A	AAB29294.1		AAB60342.1	P41002	AAH12349.1	NP_001752.1	A55501 ···	CAA85308.1	NP_002338.1			094772
						:		, , ,		•		U(C-IR) 2.52 1.60 元	ບ:(ປະວົນ) 2.12		1				U.(C-IR)	U(C-D)	U.(R.D) 2.06	
			•			: : ::	**  .	· · · · · · · · · · · · · · · · · · ·					Mm.4008.		· ,		,				Mm.2215 4	
				•	,					.4		NM_007634	NP_031660.1								NM 011837 NP 035967.1	

•	2e-54					,c			187	0		. e-180	e-111	e-1111		e-1111	e-111	e-111			c	
	209	209	209	2207		2207	2207	2202	2202	1523	687	. 630	402	402	402	402	402	402	353		1257	1257
	Ly-6 gene family~another possible initiation codon is at nt position (162164)	lymphocyte antigen 6 complex, locus H	lymphocyte antigen 6 complex, locus H	CFTR_HUMAN Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel)		cystic fibrosis transmembrane conductance regulator	cystic fibrosis transmembrane conductance regulator	cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7); cystic fibrosis transmembrane conductance regulator; ATP-binding cassette, sub-family C member 7: CFTR/MRP	cystic fibrosis transmembrane conductance regulator	transmembrane chloride conductor protein	cystic fibrosis transmembrane conductance regulator	coded for by human cDNA M96936 (NID:g180293)	Similar to ATP-binding cassette, sub-family C (CFTR/MRP), member 4	ATP-binding cassette protein C4 splice variant A	multidrug resistance-associated protein	ATP-binding cassette, sub-family C, member 4; canalicular multispecific organic anion transporter (ABC superfamily)	MRP4_HUMAN Multidrug resistance-associated protein 4 (MRP/cMOAT-related ABC transporter) (Multi-specific organic anion tranporter-B) (MOAT-B)	ABC transporter MOAT-B	ABC transporter MOAT-B isoform		caspase recruitment domain protein 14 isoform 1: CARD-containing	CARE_HUMAN Caspase recruitment domain protein 14 (CARD-containing MAGUR, protein
	BAA34115.1	AAH28894.1	AAH30192.1	P13569		DVHUCF.	AAC13657.1	NP_000483.2	AAA35680.1	AAB46352.1	AAB46340.1	AAB46341.1	AAH41560.1	AAN17334.1	AAL88745.1	NP_005836.1	015439	AAC27076.1	AAC27077.1		NP_077015.1	09BXL6
	·	٠		U:(C-IR) 2.5	U:(C-D) 2.36			•		: :	·									U:(C-IR)	U.(C-D)	
				:	Mm.1562 1				•,										: :		Mm.13083 T	
	,		· ·		NM_021050 NP_066388.1		·	: · · · · · · · · · · · · · · · · · · ·											· ·	AF363457	7.1	

	:		AAG53403.1	AF322642_1 caspase recruitment domain protein 14	1257	0
			AAK54453.1	CARD-containing MAGUK 2 protein	1257	0
		٠.	AAH18142.1	Similar to caspase recruitment domain protein 14	953	0
:			NP_438170.1	caspase recruitment domain protein 14 isoform 2; CARD-containing	407	e-113
· .	·		AAH01326.1	Unknown (protein for MGC:5551)	407	e-113
			Q9BXL7	CARB_HUMAN Caspase recruitment domain protein 11 (CARD-containing MAGUK protein	202	3e-51
	,		AAG53402.1	AF322641_1 caspase recruitment domain protein 11	202	3e-51
			NP_115791.2	caspase recruitment domain family, member 11; card-maguk protein 1;	202	
		·	AAL34460.1	AF352576_1 CARD-containing MAGUK protein CARMA1	202	
:			BAB84875.1	FLJ00120 protein	202	3e-51
NM 009203		U:(C-IR) 2.49				'
NP_033229.1	U:(C-D) Mm.12846 2.42	U:(C-D) 2.42	P_653186.2	urate anion exchanger 1 isoform a; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12	780	
			AAK68156.1	AC044790_3 RST	780	0
			BAB96750.1	URATI	780	0
			BAB68364.1	organic anion transpoter 4 like protein	889	0
			NP 060954.1	solute carrier family 22 member 11; organic anion transporter 4	502	e-142
			BAA95316.1	organic anion transporter 4	502	c-142
			AAK68155.1	AC044790_2 OAT4	505	e-142
	·		AAH34384.1	solute carrier family 22 (organic anion/cation transporter), member 11	502	e-142
	·		NP_695008.1	solute carrier family 22 member 6 isoform b; renal organic anion transporter 1; para-aminohippurate transporter	457	e-128
	,		AAD19356.1	organic anion transporter 1	457	
			BAA75073.1	hoati-2	457	e-128
· .	· ; ;		AAD55356.1	AF124373_1 organic anion transporter 1	457	· e-128
	: ;		AAH33682.1	solute carrier family 22 (organic anion transporter), member 6	457	· e-128
			AAC70004.1	putative renal organic anion transporter 1	457	e-128

solute carder family 22 member 6 isoform a; renal organic anion transporter 1;			
- 201	7	NP 004781	NP 0047
hOAT1-1		BAA75072.	BAA7507
1	_	CAB77184.	CAB7718
		AAD10052.	AAD1005
NP_700357.1  urate anion exchanger 1 isoform b; organic anion transporter 4-like; urate transporter 1; solute carrier family 22 member 12		NP_700357.	NP 700357
mic anion 'transporter 1;	sol sol	NP_695011.	NP_695011.
	1 org	BAB47393.	BAB47393.
	1 KI	NP_055643.	U:(C-IR) NP_055643. 2.47
KIAA0737 protein 891	· 🛶:	BAA34457.	BAA34457.
737 gene product	_	AAH13689.	AAH13689.
	.5 sim	XP_049037.	XP_049037.
_	•	:	
		•	
		:	
			•
		: 	
	e.		
		÷	:
FRZB_HUMAN Frizzled-related protein precursor (Frzb-1) (Frezzled) (Fritz) 6-169	· <b>E</b>	092765	U:(C-IR) Q92765 2.45
frezzled 595 e-169	ff	AAC51217.1	ÁAC51217.1
Unknown (protein for MGC:34598) e-169	$\Omega_{\mathbf{n}}$	AAH27855.1	AAH27855.1

e-169	e-169	e-169	2e-84	2e-84	0	0	0	0	e-152	e-152	e-151	e-151	e-151	e-150	e-150	e-149	e-149	e-149	e-148	e-148	e-148	2e-71	2e-71
593	593	593	312	312	1033	1033	1033	1033	536	535	534	534	532	531	530	526	526	526	523	523	523	268	268
frizzled-related protein; Friz; Frzb-1; fre; frizzled (Drosophila) homolog-related; fzrb; hfiz	Frzb precursor	Fritz	secreted frizzled-related protein 4; secreted frizzled-related protein 4	frpHE	acyl-Coenzyme A oxidase 2, branched chain; Peroxisomal branched chain acyl-CoA oxidase	CAO2_HUMAN Acyl-coenzyme A oxidase 2, peroxisomal (Branched-chain acyl-CoA oxidase) (BRCACox) (Trihydroxycoprostanoyl-CoA oxidase) (THCCox) (THCA-CoA oxidase)	branched chain acyl-CoA oxidase	peroxisomal branched chain acyl-CoA oxidase	peroxisomal acyl-coenzyme A oxidase	CAO1_HUMAN Acyl-coenzyme A oxidase 1, peroxisomal (Palmitoyl-CoA oxidase) (AOX)	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal	peroxisomal acyl-CoA oxidase	AAH08767 Similar to acyl-Coenzyme A oxidase 1, palmitoyl	AAH10425 Unknown (protein for MGC:15225)	peroxisomal fatty acyl-coA oxidase	acyl-Coenzyme A oxidase isoform b; acyl-coenzyme A oxidase 1,	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form I	acyl-CoA oxidase	acyl-Coenzyme A oxidase isoform a; acyl-coenzyme A oxidase 1	acyl-CoA oxidase (EC 1.3.3.6), peroxisomal splice form II	acyl-CoA oxidase	acyl-Coenzyme A oxidase 3, pristanoyl	CAO3_HUMAN Acyl-coenzyme A oxidase 3, peroxisomal (Pristanoyl-CoA oxidase)
NP_001454.1	AAC50736.1	AAB51298.1	NP_003005.1	AAC04617.1	NP_003491.1	099424	CAA64489.1	CAB65596.1	AAB30019.2	Q15067	. 5608EI	CAA50574.1	AAH08767.1	AAH10425.1	AAA18595.1	NP_009223.1	A54942	AAA19113.1	NP 004026,1	B54942	AAA19114.1	NP_003492.1	015254
	·			;	U:(C-IR) 2.42					```			; .			:							
	,				Mm.2870 0															. `			
	:	:	1.		NM_053115 NP_444345.1				:			.:.											

VV:	5/08	32398								191								r	CI	/0520	U3/U	033	90			
	. 20.71	e-102	100	100	201-9	e-107	e-102	701-9	2e-66	So 66	5e-66	20 00	00-00	26-00 5e 66	20.00	58-66	5e-66	18-50	10.50	0	6		0	C	0	,
	268	371	371	27.6	27.1	37.1	371	1/0	249	240	249	2/10	240	240	240	249	249	199	108	905	905	905	505	905	905	,
	pristanoyl-CoA oxidase	;	CLB2_HUMAN Calretinin (CR) (29 kDa calbindin)	calretinin	calretinin	calretinin			CABV_HUMAN Calbindin (Vitamin D-dependent calcium-binding protein, avian-type) (Calbindin D28) (D-28K)	calcium-binding protein, vitamin D-dependent	calbindin (AA 1-261)	27kDa calbindin	calbindin 1	AAH06478 calbindin 1, (28kD)			calbindin D28K	calbindin 2 isoform 22k; calbindin 2, (29kD, calretinin); calbindin D29K		٠ -	NRM1_HUMAN Natural resistance-associated macrophage protein 1 (NRAMP 1)	integral membrane protein	integral membrane protein	Nramp	natural resistance-associated macrophage protein 1	
	CAA72214.1	NP_001731.1	P22676	A60253	CAA39991.1	1709139B	AAH15484.1	NP_004920.1	P05937	S00234	CAA29860.1	AAC62230.1	AAD08724.1	AAH06478.1	AAH20864.1	1403296A	1709139A ··	NP_009019.1	NP_009018.1	XP_002585.4	P49279	155679	AAA57521.1	BAA08908.1	AAG15405.1	
		U:(C-IR) 2.42			:		: .		·	÷	·									U:(C-IR) 2.38		•	1.21			
			÷	•				:					•:		·		•			Mm.2913	• ;					•
					•			٠						•						NM_013612 NP_038640.1		·.	٠.			:

		:	BAA08907.1	Nramp	904	C
			JC4095	natural resistance-associated macrophage protein NRAMP 1	688	0
	, *. ,	· :	NP_000569.1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1; natural resistance-associated macrophage protein 1 (might include Leishmaniasis).	887	0.
•			.:	solute carrier family 11 (sodium/phosphate symporters), member 1		•
		: :	CAA57541.1	NRAMP	887	0
			BAA07370.1	Nramp	818	°
		.:	CAD38517.1	divalent metal transporter	649	0
	· · ·	·	NP_000608.1	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2; natural resistance-associated macrophage protein 2	649	0
•	·		BAA24933.1	NRAMP2	649	О.
		•	AAC21460.1	natural resistance-associated macrophage protein 2	649	0
			AAC18078.1	NRAMP2 iron transporter	649	92
			AAH02592.1	AAH02592 solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	649	0
			P49281	NRM2_HUMAN Natural resistance-associated macrophage protein 2 (NRAMP 2) (Divalent metal transporter 1) (DMT1)	. 648	0
*:	:		AAC21459.1	natural resistance-associated macrophage protein 2 non-IRB form	648	0
			AAC21461.1	natural resistance-associated macrophage protein 2	. 648	0
			BAB93467.1	natural resistance-associated macrophage protein 2 non-IRE form	648	0
.	·		BAA34374.1	natural resistance-associated macrophage protein 2	633	0
:			I57022	integral membrane protein	629	· e-180
		,	AAA79219.1	integral membrane protein	629	e-180
NM_020503 NP_065249.1	Mm.1038 03	U:(C-IR) 2.38	NP_062545.1	taste receptor T2R1; taste receptor, family B, member 7; taste receptor, type 2, member 1	. 260	2e-69
		·	AAF43902.1	AF227129_1 candidate taste receptor T2R1	260	2e-69
NM_026091 NP_080367.1	Mm.2771	U:(C-R) 2.36	BAB14854.1	unnamed protein product	323	4e-88
: '	.:		CAC17545,1	d/1009E24.3 (novel protein)	323	4e-88

-									193	,													
40.88	46-88	10.87	16.87	10-01			0		0	0	8e-91	8e-91	. 8e-91	86-91	20.83	2e-83	2e-83	2e-83	2e-83	2e-83	2e-83	4e-75	4e-75
222	323	33	331	1777		629	679	673	673	673	332	332	332	332	308	308	308	308	308	308	308	280	280
AAH12196 Unknown (protein for MGC:4349)	chromosome 20 open reading frame 27	chromosome 20 open reading frame 27	unnamed protein product			CXA8_HUMAN Gap junction alpha-8 protein (Connexin 50) (Cx50) (Lens fiber protein MP70)	AF217524_1 gap junction protein alpha 8	gap junction protein, alpha 8, 50kDa (connexin 50); gap junction membrane channel protein alpha-8; connexin 50; Gap junction membrane channel protein alpha-8 (connexin 50); gap junction protein, alpha 8, 50kD (connexin 50)	intrinsic membrane protein MP70	gap junction membrane channel protein alpha-	gap junction protein, alpha 3, 46kDa (connexin 46); gap junction protein, alpha 3, 46kD (connexin 46)	bA26414.3 (novel connexin (gap junction protein))	CXA3_HUMAN Gap junction alpha-3 protein (Connexin 46) (Cx46)	gap-junction protein alpha 3	gap junction protein, alpha 5, 40kDa (connexin 40); gap junction protein, alpha 5, 40kD (connexin 40)	CXA5_HUMAN Gap junction alpha-5 protein (Connexin 40) (Cx40)	comexin 40	AF151979_1 connexin 40	connexin40	AAH13313 gap junction protein, alpha 5, 40kD (connexin 40)8	connexin40	AF271261_1 connexin 58	connexin 59; gap junction alpha 10
AAH12196.1	AAH24036.1	NP_060344.1	BAA91252.1	: :	· · .	 P48165	AAF32309.1	NP_005258.1	139176	AAA77062.1	NP_068773.2	CAC16957.1	09У6Н8	AAD42925.1	NP_005257.2	P36382	AAA91833.1	AAD37801.1	AAA60457.2	AAH13313.1	I38429	AAK55516.1	NP_110399.1
•	•				- - - -	U:(C-IR) 2.35	':										: • •						
:	:		•			U:(C Mm.56907 2.35																	
					NM_008123	· 🛶					, ,								:				

		;			•
	· :	P57773	CXAA_HUMAN Gap junction alpha-10 protein (Connexin 59) (Cx59)	280	4e-75
		AAG09406.1	AF179597_1 connexin 59	280	4e-75
		NP_115991.1	connexin 62	279	8e-75
1		AAK51676.1	AF296766_1 connexin 62	279	8e-75
	·	CAC93847.1	connexin62	279	8e-75
		AAD56533.1	AF180815_1 truncated connexin 37 polymorph	267	3e-71
NM_013473 NP_038501.2 Mm.3267	U:(C-IR) 2.35	XP_036593.2	similar to annexin A8	296	e-170
	٠	AAH04376.1	AAH04376 annexin A8	596	e-170
·		NP_001621.1	annexin VIII; Annexin VII	595	e-169
		P13928	ANX8_HUMAN Annexin A8 (Annexin VIII) (Vascular anticoagulant-beta) (VAC-beta)	595	e-169
	:	CAA34650.1	vascular anticoagulant-beta (AA 1 - 327)	595	94
:		LUHU8	amexin VIII	593	e-169
	·	AAB46383.1	anexin VIII	590	e-168
		XP_054475.4	similar to annexin A8	575	e-165
		P09525.	ANX4_HUMAN Annexin A4 (Annexin IV) (Lipocortin IV) (Endonexin I) (Chromobindin 4) (Protein II) (P32.5) (Placental anticoagulant protein II) (PAP-II) (PP4-X) (35-beta calcimedin) (Carbohydrate-binding protein P33/P41) (P33/41)	337	4e-92
		NP_001144.1	annexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
		XP_031596.2	similar to amexin IV; annexin IV (placental anticoagulant protein II); placental anticoagulant protein II	337	4e-92
		A42077	annexin IV	337	4e-92
	·	AAA51740.1	annexin IV (placental anticoagulant protein II)	337	4e-92
		BAA11227.1	annexin IV (carbohydrtate-binding protein p33/41)	337	4e-92
٠.		AAH00182.1	AAH00182 annexin A4	337	4e-92
.		AAH11659.1	AAH11659 Similar to annexin A4	337	4e-92
		AAC41689.1	protein PP4-X	337	4e-92

0	76-82	69-97				0		0	0	0	0		20 00	2e-85	20.00	26-65	28.95	16-84	2e-82	26-82	2e-82	2e-81
000	370	970		600	001	88	739	654	659	652	652	160	4.39	315	215	315	315	312	305	305	305	302
calphobindin	coagulation inhibitor		gamma-aminobutyric acid (GABA) receptor, rho 1; gamma-aminobutyric acid (GABA) A receptor, rho-1	GAR1_HUMAN Gamma-aminobutyric-acid receptor rho-1 subunit precursor (GABA(A) receptor)	gamma-aminobutyric acid receptor A rho-1 chain precursor	gamma-aminobutyric acid receptor type A rho-1 subunit	GAR2_HUMAN Gamma-aminobutyric-acid receptor rho-2 subunit precursor. (GABA(A) receptor)	dJ131H7.1 (gamma-aminobutyric acid (GABA) receptor rho 2)	gamma-aminobutyric acid (GABA) receptor, rho 2 precursor	gamma-aminobutyric acid receptor rho-2 chain precursor	gamma-amino butyric acid	similar to Gamma-aminobutyric-acid receptor rho-3 subunit precursor (GABA(A)		gamma-aminobutyric acid (GABA) A receptor, beta 3, isoform 1 precursor	GABA HUMAN Gamma-aminobutyric-acid receptor beta-3 subunit precursor (GABA(A) receptor)	gamma-ammobutyric acid A receptor beta 3 chain splice form 1	GABA-alpha receptor beta-3 subunit	gamma-aminobutyric acid (GABA) A receptor, beta 3	gamma-aminobutyric acid (GABA) A receptor, delta	GAD_HUMAN Gamma-aminobutyric-acid receptor delta subunit precursor (GABA(A) receptor)	GABA-A receptor delta subunit	gamma-aminobutyric acid (GABA) A receptor, delta
1512315A	1313303A		NP_002033.1	P24046	A38627	AAA52509.1	P28476	CAC07339.1	NP_002034.1	A38079	AAA52510.1	XP 116036.2		NP_000805.1	P28472	A55275.	AAA52511.1	AAH10641.1	NP_000806.1	014764	AAB70007.1	AAH33801.1
	,		U:(C-R) 2.33	٠			•	·										:.· :	:		:	
			Mm.14116	1					:		.:	. ,			·. ·		! `	•			:	
	3	NM_008075	NP_032101.1 Mm.14116 2.33	:				r.				:					*	V	: ::.		7 ·	

, 20	05/0	02070								197						_				_	
	· 2e-81	2e-81	2e-81	.2e-81		2e-71	2e-71	2e-71	. 2e-71	2e-71	2e-71	e-120	e-120	e-120	e-120	e-120	e-120	e-120	. e-120	e-111	e-111
	302	302	302	302		268	268	268	268	268	268	431	431	431	431	431	431	. 431	429	400	400
	garnma-aminobutyric acid (GABA) A receptor, beta 2, isoform 2	GAB2_HUMAN Gamma-aminobutyric-acid receptor beta-2 subunit precursor (GABA(A) receptor)	gamma-aminobutyric acid A receptor beta 2 subunit; (GABA)A receptor beta 2 subunit	GABAA receptor beta 2 subunit		heparin-binding growth factor binding protein	heparin-binding growth factor-binding protein precurso	heparin binding protein	AF149412_1 HBP17 heparin-binding and FGF-binding protein	heparin-binding growth factor binding protein	heparin-binding growth factor binding protein	interleukin 12B precursor; natural killer cell stirmlatory factor-2; interleukin 12B; cytotoxic lymphocyte maturation factor 2, p40; interkeukin-12 beta chain; interleukin 12, p40; natural killer cell stimulatory factor, 40 kD subunit, II.23, subuint p40	H H O	interleukin 12B precursor	cytotoxic lymphocyte maturation factor 40 kDa subunit	AF180563_1 interleukin 12, P40	interleukin 12 p40 subunit	AF\$12686_1 interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40)	natural killer cell stimulatory factor	A Chain A, The P40 Domain Of Human Interleukin-12	A Chain A, Human Interleukin-12
	NP 000804.1	 P47870	AAB29370.1	AAB33983.1	<i>t.</i>	NP_005121.1	A41178	AAA58636.1	AAD39216.1	AAH03628.1	AAH08910.1	NP 002178.2	P29460	A38957	AAA35695.1	AAD56386.1	AAG32620.1	AAM34792.1	AAA59938.1	1F42	1F45
						U:(C-IR) 2.32		·			. •	U:(C-IR) 2.29 U:(C-D) 2.24			••					·	
::						U;(C Mm.46053 2.32		•										·.		•	
					IM 008009	IP_032035.1						TM_008352	:				;			V :: :	

5e-61	3e-56
234	178
small integral membrane protein of lysosome/late endosome	LPS-induced TNF-alpha factor
U:(C-IR) BAB32547.1 2.28 U:(C-D) 2.11	NP 004853.1
U:(C-IR) 2.28 U:(C-D) 2.11	,
Mm.2111 9	
NM_019980 Mm.2111 U.(C-D) NP_064364.1 9 2.11	

	.					
			Q99732	I.ITF_HUMAN Lipopolysaccharide-induced tumor necrosis factor-alpha factor (LPS-induced TNF-alpha factor) (P53-induced protein 7)	178	3e-56
		·	AAB36550.1	LPS-Induced TNF-Alpha Factor	178	30.56
			AAC39530.1	Pig7	170	30.50
					\$	26-30
·			:			
		:			<u> </u>	
		U:(C-IR)	AAH22393.1	teratocarcinoma-derived growth factor 1	239	1e-62
NM_011562 NP_035692.1	Mm.5090	2.28 U:(C-D) 2.03				
:			NP_003203.1	teratocarcinoma-derived growth factor 1	738	20.62
			P13385	CRI1_HUMAN Teratocarcinoma-derived growth factor 1 (Epidernal growth factor-like cripto protein CR1) (Cripto-1 growth factor) (CR CR)	. 238	199 79-97 79-97
: : :			A30362	teratocarcinoma-derived growth factor 1	, 720	2,5 67
;			CAA32467.1	cripto protein (AA 1-188)	220	70-27
			AAA61134.1	teratocarcinoma-derived growth factor 1	230	70-97
		. ,	P51864	CRI2_HUMAN Teratocarcinoma-derived growth factor 2 (Bpidermal growth	235	2e-07
			A A A 61135 1	lactor-like cripto protein CR3) (Cripto-3 growth factor)		1
			1,00110000	teratocatchoma-denyed growth factor 3	235	2e-61
			AAB46353.1	EGF repeat containing protein; HUMTDGF1A Human (clone CR) teratocarcinoma-derived growth factor 1 (TDGF1) gene P13385; coded for by human cDNAs M96956 (NID:g339432), X14253 (NID:g30220) and M96955 (NID:g339430).	235	2e-61
:			AAG49538.1	AF251549 1 cripto 3	23.5	20.61
			AAG49539.1	AF251550_1 cripto 3	235	20-61
		• .	A39787	teratocarcinoma-derived growth factor	225	70 61
***		:: ::	XP_092153.1	similar to teratocarcinoma-derived growth factor 1	202	10 02 P
NM_019871 NP_063924.1	Mm.6211	U:(C-IR) 2.27	XP_083967.1	similar to acyl-malonyl condensing enzyme	186	5e-88
			NP 689675.1	hypothetical protein FLJ40154	186	5e-88

_										20	0															
	5e-88	2e-87	2e-85	20.85	70.02	Co-5/							C	°	-	2 6	0	e-103	e-103	e-102	1e-72	76-71				0
	186	184	182	182	18	707							1170	1170	1167	1167	1163	375	375	371	270	7,064		1405	1493	1379
	٦.	2 similar to acyl-malonyl condensing enzyme	1 acyl-malonyl condensing enzyme									AKA3_HUMAN A-kinase anchor protein 3 (Protein kinase A anchoring protein	3)(PKKA3) (A-kinase anchor protein 110 kDa) (AKAP 110) (Sperm oocyte binding protein) (Fibrousheathin I) (Fibrous sheath protein of 95 kDa) (FSP95	protein kinase A binding protein AKAP110			_	l kinase (PRKA) anchor protein 4 isoform 2; A-kinase anchor protein 82 kd	? A kinase (PRKA) anchor protein 4 isoform 1; A-kinase anchor protein 82 kDa	major sperm fibrous sheath protein precursor	sperm protein	A-kinase anchoring protein homolog		KIAA1220 protein	_	
1 1 COSOC 1	DAC0300/.1	XP_083960.2	NP_473369.1	CAC82744.1	XP 064583.3	: !		<i>:</i>		. ,			075969	AAC63371.1	AAD21218.1	NP_006413.2	AAC35854.1	NP_647450.1	NP_003877.2	AAC79433.1	CAA75494.1	JC5986		BAA86534.1	XP 043613.7	*****
			•				·.				71.(7.10)	2.26 2.26	(עי							•				U:(C-IR) 2.26		
						:						.;	Mm.87748				٠.	,						Mm.7983	· ·	
			;								.,	NM_009650	NP 033780.1	·.						. 1		·	NM_008166	NP_032192.1	;	

	201	
0 0 0 0 2e-99	2e-99 2e-99 2e-99 8e-98 1e-94 5e-94 e-124	e-124 e-124 e-124 e-124 e-124 e-124 1e-97 3e-66 6e-66
1202 1141 1141 362	362 362 359 357 346 344 344	442 442 442 442 442 250 250 249
<ul> <li>Similar to glutamate receptor, ionotropic, delta 1</li> <li>glutamate receptor, ionotropic, delta 2; GluR-delta-2</li> <li>GRD2_HUMAN Glutamate receptor delta-2 subunit precursor</li> <li>glutamate receptor delta-2 subunit</li> <li>glutamate receptor, ionotropic, kainate 1; human glutamate receptor (GLUR5)</li> <li>GLK1 HUMAN Glutamate receptor, ionotropic kainate 1 precursor (Glutamate</li> </ul>		SNAI HUMAN Zinc finger protein  SNAI HUMAN Zinc finger protein SNAII (Snail protein homolog) (Sna protein)  AF155232 I snail zinc finger protein  AF151208 I snail I (drosophila homolog), zinc finger protein  AF131208 I snail protein  AF131208 I snail protein  Protein  SLUG HUMAN Zinc finger protein SLUG (Neural crest transcription factor Slug)  (Snail homolog 2)
AAH39263.1 NP_001501.1 O43424 AAC39579.1 NP_000821.1	P39086 158178 AAA52568.1 CAC80546.1 AAA95961.1 CAC80548.1 NP_000822.1 AAB60407.1 AAD17332.1	NP 005976.2 095863 CAB52414.1 AAD52986.1 CAC07340.1 AAH12910.1 XP 065615.1 NP 003059.1
	U:(C-IR)	
		كالت المصابقة والتناسي بالألة ليني المهر بيها والت النبية النبية النبية المناه
	NM 011427 NP 035557.1	

			AAD55240.1	AF084243 1 zinc finger protein STITG	9,0	
			AAH14890.1	AAH14890 slug (chicken homolog), zinc finger protein	240	99-99
			AÁH15895.1	AAH15895 slug (chicken homolog), zinc finger protein	249	99-99 99-99
NM_021546 NP_067521.1	Mim.1437 48	U:(C-IR) 2.26	AAL01118.1	AF409141_1 NIP1	477	e-134
		:	NP_112508.1	amyloid beta (A4) precursor protein-binding, family A, member 2 binding protein, isoform 1; synaptotagmin interacting protein STIP3; X11L-binding protein 51; amyloid beta (A4) precursor protein-binding, family A, member 2; synaptotagmin interacting protein 2; neuronal calcium-binding protein NECAB3	475	e-134
			AAG28415.1	AF193759_1 neuronal calcium binding protein NECAB3	475	e-134
	·		CAD37360.1	d163M2.4.1 (amyloid beta (A4) precursor protein-binding family A, member 2 protein, variant 1)	397	e-110
	:		NP_112509.1	amyloid beta (A4) precursor protein-binding, family A, member 2 binding protein, isoform 2; synaptotagmin interacting protein STIP3; X11L-binding protein 51; amyloid beta (A4) precursor protein-binding, family A, member 2; synaptotagmin interacting protein 2; neuronal calcium-binding protein NECAB3	358	202   86   87
:	· · ;		BAB16413.1	X11L-binding protein 51	358	2e-98
:: ,			NP 071746.1	synaptotagmin interacting protein 1	254	3e-67
			BAC04568.1	unnamed protein product	254	3e-67
			AAG28412.1	AF193756_1 neuronal calcium binding protein NECAB1	196	7e-50
NM_025746 NP_080022.1	Mm.4614 2	U:(C-IR) 2.24	2208307A	PNG gene	206	9e-53
		. 1				
		:				:
•						
AAN60072.1	Mm.29522	2.23	AAL23683.1.	MARK4 serine/threonine protein kinase	183	9e-51
	• : 1		BAC11510.1	unnamed protein product	183	9e-51
			AAM55491.1	MAP/microtubule affinity-regulating kinase-like 1	183	9e-51
:			BAC03375.1	microtubule affinity-regulating kinase-like1	183	9e-51
	!					

102 02 51			506 e-143	····	506 6-143	e-143 e-143	e-143 e-143	e-143 e-143 e-143	e-143 e-143 e-143 e-143	e-143 e-143 e-143 e-143 e-143	e-143 e-143 e-143 e-128 1e-90	e-143 e-143 e-143 e-143 e-128 1e-90 1e-90	e-143 e-143 e-143 e-128 1e-90 1e-90 3e-80	e-143 e-143 e-143 e-143 e-128 1e-90 1e-90 1e-70	e-143 e-143 e-143 e-128 le-90 1e-90 3e-80 1e-70	e-143 e-143 e-143 e-143 e-128 1e-90 1e-70 1e-70 1e-70	e-143 e-143 e-143 e-143 e-128 1e-90 3e-80 1e-70 4e-67 9e-67	e-143 e-143 e-143 e-143 e-128 1e-90 3e-80 1e-70 4e-67 9e-67	e-143 e-143 e-143 e-143 e-143 e-128 1e-90 1e-70 1e-70 9e-67 9e-67	e-143 e-143 e-143 e-143 e-128 1e-90 3e-80 1e-70 4e-67 9e-67	
-	15.	•	<u> </u>		5	5	5.	4	3	. 3	2			7	7 2	7 7 7	7 7 7 8				
umamed protein product	l beta-1,3-N-acetylglucosaminyltransferase bGnT-3		<ol> <li>beta-1,3-N-acetylglucosaminyltransferase bGnT-3; type II membrane protein;</li> <li>transmembrane protein 3; core 1 extending beta-1,3-N-acetylglucosaminyltransferase;</li> <li>beta-1,3-galactosyltransferase;</li> <li>beta-1,3-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase 8;</li> <li>beta-3-GX-T8</li> </ol>	B3G8_HUMAN Beta-1,3-galactosyltransferase & (Beta-1,3-GalTase &) (Beta3Gal-T8) (b3Gal-T8) (UDP-galactose:beta-N-acetylglucosamine beta-1,3-galactosyltransferase &) (UDP-Gal:beta-GlcNAc beta-1,3-galactosyltransferase &) (Beta-3-Gx-T8) (Core 1 extending beta-1,3-N-acetylglucosaminyltransferase) (Core1-beta3GlcNAcT)		AF293973 1 core 1 extending beta-1,3-N-acetylglucosaminyltransferase		beta 1,6-GlcNAc-transferase	1 beta-1,3-N-acetylglucosaminyltransferase protein	beta-1,3-N-acetylglucosaminyltransferase 6	Unknown (protein for IMAGE:4907098)	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7; hypothetical gene supported by AK000770	1 AF502430 1 beta 1,3-N-acetylglucosaminyltransferase 7	_	beta-1,3-galactosyltransferase						
BAB21531.1		1	NP_055071.1 t		BAA76497.1 t	AAK00849.1	CAC45044.1	CAC82374.1	NP 619651.1 E	BAB88882.1 b	AAH25357.1 U	NP_660279.1 U	AAM61770.1	CAC45045.1 b		BAC04622.1 u					
	U:(C-IR) 2.22	U.(C-IR) 2.41						-				. :									U:(C.IR)
		Mm.2885 6		1.		. ;	;				·	:	. :							6 1 1	8 1 1 6
	: · · · · · · · · · · · · · · · · · · ·	NM 028189 NP 082465.1						* .											NM_008522	NM_008522	NM_008522 NP_032548.1 Mm.7612

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TRFL HUMAN Lactotransferrin precursor (Lactoferrin) [Contains: Lactoferroxin A;	TACKOLLIAMIL D. LACIDICII OXIII C.	lactotransferrin precursor	l lactoferrin	lactotransferrin	l lactotransferrin	precursor lactoferrin (709 AA)	l lactoferrin	l lactoferrin	lactoferrin	l lactoferrin precursor	lactotransferrin precursor	l lactotransferrin	1 lactotransferrin	precursor (AA -19 to 692)		similar to AE binding protein 2. AR-hinding protein 2			Unknown (protein for MGC; 17922)		FGFB_HUMAN Fibroblast growth factor-11 (FGF-11) (Fibroblast growth factor homologous factor 3) (FHF-3)	fibroblast growth factor homologous factor 3	fibroblast growth factor 11	1 fibroblast growth factor 11	
D0.7788	102/00.	1FHUL .	AAB60324.1	AAH15822.1	AAH22347.1	CAA37116.1	AAA36159.1	AAN11304.1	AAA59511.1	AAG48753.1	AAN63998.1	AAH15823.1	NP_002334.1	CAA37914.1-	,	XP 058567.1	NP 694939.1	AAH15624.1	AAH22220.1	NP_004103.1	092914	AAB18915.1	AAL15439.1	AAM11871.1	A A 1732502 1
							•			:				•	•	U:(C-IR) 2.22				U:(C-IR) 2.22	;			:	
								1.44					:	.;		U:(( Mm.86453 2.22	.:			Mm.5723 8					•
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16-73	1e-73	1e-73	1e-73	2e-73	2e-73	2e-73	5e-70	26-65	2e-65	- 2e-65	2e-65	2e-65	2e-65	2e-58	7e-58	7e-58	. 2e-57	1e-55	1e-55
. 273	273	273	.273	273	273	273	261	246	246	246	246	246	246	223	221	. 221	219	213	213
fibroblast growth factor 14; fibroblast growth factor homologous factor 4	FGFE_HUMAN Fibroblast growth factor-14 (FGF-14) (Fibroblast growth factor homologous factor 4) (FHF-4)	fibroblast growth factor homologous factor 4	AE014303_1_FHF4	fibroblast growth factor 12 isoform 1; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	FGFC_HUMAN Fibroblast growth factor-12 (FGF-12) (Fibroblast growth factor homologous factor 1) (FHF-1) (Myocyte-activating factor)	fibroblast growth factor homologous factor 1	fibroblast growth factor 11	fibroblast growth factor 13, isoform 1A; fibroblast growth factor homologous factor 2	FGFD_HUMAN Fibroblast growth factor-13 (FGF-13) (Fibroblast growth factor homologous factor 2) (FHF-2)	fibroblast growth factor homologous factor 2	fibroblast growth factor 13 isoform 1A	AAH12347 Unknown (protein for MGC:20109)	fibroblast growth factor 13	fibroblast growth factor 12 isoform 2; fibroblast growth factor homologous factor 1; myocyte-activating factor; fibroblast growth factor 12B; fibroblast growth factor FGF-12b	fibroblast growth factor - human	fibroblast growth factor	Unknown (protein for MGC:26659)	fibroblast growth factor 13 isoform 1B; fibroblast growth factor homologous factor 2	fibroblast growth factor 13 isoform 1B
NP 004106.1	Q92915	AAB18916.1	AAN16025.1	NP_066360.1	Q92912	AAB18913.1	CAA94239.1	NP_004105.1	Q92913	AAB18914.1	AAD16400.1	AAH12347.1	ААН34340.1	NP_004104.3	JG0184	AAB18786.3	AAH22524.1	NP_378668.1	AAD16401.1
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	· e-107	e-107	e-107	e-107	e-106	e-106	e-105	e-105	P-105	e-105	66-97	5e-78	5e-78	5e-78	2e-75	2e-75	7e-62	1e-55	1e-55	1e-55	1e-55	1
	386	386	386	386	382	382	379	379	3,78	379	352	289	289	289	281	281	.236	215	215	215	215	
	ficolin 1 precursor; ficolin (collagen/fibrinogen domain-containing) 1	FCN1_HUMAN Ficolin 1 precursor (Collagen/fibrinogen domain-containing protein 1) (Ficolin-A) (Ficolin A) (M-Ficolin)	ficolin (collagen/fibrinogen domain-containing) 1	ficolin	ficolin-1 precursor	ficolin	ficolin 2 isoform a precursor; ficolin (collagen/fibrinogen domain-containing lectin) 2 (hucolin); ficolin (collagen/fibrinogen domain-containing lectin) 2; hucolin	FCN2_HUMAN Ficolin 2 precursor (Collagen/fibrinogen domain-containing protein 2) (Ficolin-B) (Ficolin B) (Serum lectin p35) (EBP-37) (Hucolin) (L-Ficolin)	serum lectin P35	lectin P35	ficolin 2 isoform b precursor; ficolin (collagen/fibrinogen domain-containing lectin) 2 (hucolin); ficolin (collagen/fibrinogen domain-containing lectin) 2; hucolin		FCN3_HUMAN Ficolin 3 precursor (Collagen/fibrinogen domain-containing protein 3) (Collagen/fibrinogen domain-containing lectin 3 p35) (Hakata antigen)	Hakata antigen	Similar to ficolin (collagen/fibrinogen domain-containing) 3 (Hakata antigen)	unnamed protein product	Unknown (protein for MGC:33476)	similar to Microfibril-associated glycoprotein 4	microfibrillar-associated protein 4; microfibril-associated glycoprotein 4	MFA4_HUMAN Microfibril-associated glycoprotein 4 precursor.	microfibril-associated glycoprotein 4	
	NP_001994.2	000602	A:AH20635.1	BAA12120.1	S61517	AAB50706.1	NP 004099.1	Q15485	BAA08352.1	BAA09636.1	NP_056652.1	NP_003656.1	075636	BAA32277.1	AAH20731.1	BAC11429.1	AAH32953.1	XP 045044.2	NP 002395.1	P55083	AAB00968.1	
U:(C-IR) 2.21	U:(C-D) 2.45		. :							٠;		·. : :				· .						
	Mm.10510			,				:			: <b>∶</b> :									:!		
NM_007995	NP 032021.1 Mm.10510 2.45		 				· 1	: '														

· ·
hypothetical protein FLJ32702 unnamed protein product
unnamed protein product
nnamed protein
U.(C.IR) XP 032835
:

	26-52	5e-52	· e-118		110	6-110	6-118	26-69		2e-69	300	200	76-03	3e-55		36-93	3e-93	50-93	2e-6/	20.70	26.70	26-79
	203	203	. 424		707	177	177	259		259	250	65.5	607	212		240	340	310	293	203	203	293
testis sodium channel 1	sodium chamel	_	Claudin 18		CLDI HUMAN Claudin-18	AF221069 1 Claudin-18	AF349452 1 claudin-18A2 1	retinoid binding protein 7; putative cellular retinol-binding protein CRBP IV		RET7_HUMAN Retinol-binding protein IV, cellular (CRBP-IV) (Retinoid binding protein 7)	retinoid binding protein 7	putative cellular retinol-hinding protein CRRP IV	Similar to refincid hinding anothein 7	omina to remove omining protein /	cell death-inducino DFFA-like effector o	CIDA_HUMAN Cell death activator CIDE-A (Cell death-inducing DFFA-like	cell death activator CDR-A	Similar to cell death-inducing DFFA-like effector a	hypothetical protein MGC861	hypothetical protein	AAH00705 Unknown (protein for MGC:861)	AAH07495 hypothetical protein MGC861
JE0091	BAA25897.1	ATT OFFICE .	INF_U3/453.1	· :	P56856	AAF26448.1	AAL15637.1	NP_443192.1		Q96R05	AAK85409.1	AAN61071.1	AAH33883 1		NP 001270.1		AAC34987.1	AAH31896.1	U:(C-IR) NP_076958.1 2.16	CAB77147.1	AAH00705.1	AAH07495.1
		11.03	2.13	U:(C-D) 2.12		, 	. '	眾	U:(C-D) 2.04						U:(C-IR) 2.16	: : 			U:(C-IR) 2.16		: :	·
			: .	Mm.3509 1					Mm.4602 3	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \					 Mm.449				Mm.2359 6		***************************************	
	.*		:	NM_019815 NP_062789.1		:: :: ::		. 5	NIM_022020 NP_071303.1					NN 007702	NP 031728.1				NM_025639 NP_079915.1			• •

e-159	0-150	0.150	4 150	6-150	6-156	e-156	e-156	e-127	7e-55	7e-55	1e-54	16-54	10.54	16-54	1e-54	1e-54	1è-54	6e-51	6e-5 <u>1</u>	. 6e-51	6e-51	6e-51	6e-51	6e-51
260	560	260	260	560	550	550	550	454	. 214	214	213	213	213	213	· 213	213	213	201	201	201	201	201	201	201
protein Z, vitamin K-dependent plasma glycoprotein	PRTZ_HUMAN Vitamin K-dependent protein Z precursor	protein Z	protein Z.	AF440358_1 protein Z, vitamin K-dependent plasma glycoprotein	plasma protein Z precursor	protein Z.	protein Z spliced variant	protein Z	coagulation factor X precursor	coagulation factor X	factor X prepeptide	coagulation factor X precursor; Prothrombinase	FA10_HUMAN Coagulation factor X precursor (Stuart factor)	coagulation factor Xa (BC 3.4.21.6) precursor	coagulation factor X	coagulation factor X	AF503510_1 coagulation factor X	F9 (coagulation factor IX (plasma thromboplastic component, Christmas disease,haemophilia B))	coagulation factor IX; Coagulation factor IX (plasma thromboplastic component); Factor 9; Factor IX; Christmas factor	coagulation factor IX precursor	factor IX (Christmas factor) precursor	coagulation factor IX (plasma thromboplastic component, Christmas disease, hemophilia B)	FA9_HUMAN Coagulation factor IX precursor (Christmas factor)	coagulation factor IXa (BC 3.4.21.22) precursor
NP_003882.1	P22891	AAA36500.1	BAA85763.1	AAL27631.1	KXHUZ .	AAA36501.1	BAA85764.1	AAA36499.1	AAA51984.1	1205236A	AAA52490.1	NP_000495.1	P00742	EXHU	AAA52421.1	AAA52764.1	AAM19347.1	CAA21954.1	NP_000124.1	AAA52023.1	AAA52763.1	AAM96188.1	P00740	KPHÚ .
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Mm.8079 U:(C-IR) 8 2.16							:					. ,				•	:	: "						
NM_025834 NP_080110.1							,			:				·	•			:						

1.			AAR59620 1	Parton IV		
			7 0 0 0 0 7 9 V V	TOWN TAX	201	6e-51
			AAA30822.1	ractor LX	201	6e-51
40,00			AAA98726.1	factor IX	199	3e-50
AAC52197.1	Mm.2212	U:(C-IR) 2.16	DAHUAI	procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 1	1001	0
		: .	AAA59069.1	alpha-subunit of prolyl 4-hydroxylase	5	
			NP_000908.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I; procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide 1	991	
	:		AAA36534.1	prolyl 4-hydroxylase alpha subunit (BC 1.14.11.2)	166	0
			P13674	P4H1_HUMAN Prolyl 4-hydroxylase alpha-1 subumit precursor (4-PH alpha-1) (Procollagen-proline, 2-oxoglutarate-4-dioxygenase alpha-1 subumit)	982	0
		. :	DAHUA2 .	procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 2	982	c
		·	AAA59068.1	alpha-subunit of prolyl 4-hydroxylase	982	0
,			AAH34998.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I	982	0
			AAA36535.1	prolyl 4-hydroxylase alpha submit (BC 1.14.11.2)	971	0.
			NP_004190.1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II; prolyl 4-hydroxylase, alpha polypeptide, type II	629	0
			015460	P4H2_HUMAN Prolyl 4-hydroxylase alpha-2 subunit precursor (4-PH alpha-2) (Procollagen-proline, 2-oxoglutarate-4-dioxygenase alpha-2 subunit)	629	0
			AAB71339.1	prolyl 4-hydroxylase alpha (II) subunit	629	0
:		·	CAC85689.1	Prolyl 4-hydroxylase alpha IIb subunit	679	0
			-	Prolyl 4-hydroxylase alpha IIa subunit	658	0
	, · :		AAH35813.1	Similar to procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II	859	0
		U:(C-R)	NP_002603.1	pyruvate dehydrogenase kinase, isoenzyme 4	764	0
NM_013743 NP_038771.1	Mm.1028 3		 .:		:	

			016654	PDZ4 HIMAN Branch 1.1.1		
1			i constant	mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 4)	764	0
1:	.:-		AAC50669.1	pyruvate dehydrogenase kinase isoform 4	764	6
			AAC50670.1	pyruvate dehydrogenase kinase isoform 4	764	
			AAB67048.1	pyruvate dehydrogenase kinase isoform 4	764	
.:			AAH40239.1	pyruvate dehydrogenase kinase, isoenzyme 4	764	
			NP_002601.1	pyruvate dehydrogenase kinase, isoenzyme 1	567	. 2.150
		:	Q15118	PDK1_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 1, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 1)	562	e-159
		•	I55465	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99) 1	562	e-159
			AAC42009.1	pyruvate dehydrogenase kinase	562	
		·	AAH39158.1	Similar to pyruvate dehydrogenase kinase, isoenzyme 1	562	e-159
	<i>‡</i>	•	2203383A	pyruvate dehydrogenase kinase:ISOTYPE=1	562	e-159
		•	NP_002602.2	pyruvate dehydrogenase kinase, isoenzyme 2.	556	e-157
			Q151 <u>19</u>	PDK2_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 2, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 2)	556	e-157
		·	AAH05811.1	AAH05811 pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
3			AAH40478.1	pyruvate dehydrogenase kinase, isoenzyme 2	556	e-157
		^.	170159	[pyruvate dehydrogenase (lipoamide)] kinase (BC 2.7.1.99) 2	554	e-157
			AAC42010.1	pyruvate dehydrogenase kinase	554	e-157
			2203383B	pyruvate dehydrogenase kinase:ISOTYPB=2	554	e-157
			NP_005382.1	pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
			Q15120	PDK3_HUMAN [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 3, mitochondrial precursor (Pyruvate dehydrogenase kinase isoform 3)	527	e-149
			170160	[pyruvate dehydrogenase (lipoamide)] kinase (EC 2.7.1.99).3	527	e-149
			AAC42011.1	pyruvate dehydrogenase kinase	527	e-149
\$ 12.1 12.1 13.1 14.1 15.1	:; ::		AAH15948.1	AAH15948 pyruvate dehydrogenase kinase, isoenzyme 3	527	e-149
		:	2203383C	pyruvate dehydrogenase kinase:ISOTYPE=3	527	· e-149

- 1						
U:(C	U:(	U:(C-IR) 2.15	NP_079105.1	hypothetical protein FL J22662	870	0
			BAB15442.1	unnamed protein product	870	
	,		AAH00909.2	AAH00909 hypothetical protein FLJ22662	3 6	6-110
:	ı,		XP_113725.2	similar to RIKEN cDNA 1300012G16	271	2e-72
:	:-		AAH30618.1	similar to RIKEN cDNA 1300012G16	27.	20-77
<u>₽</u>	2	U:(C-IR) 2.14	. ! 			
Mm.2900 2	<u> 고</u>	U:(C-D) 2.22	P31513	FMO3_HUMAN Dimethylaniline monooxygenase [N-oxide forming] 3 (Hepatic flavin-containing monooxygenase 3) (FMO 3) (Dimethylaniline oxidase 3) (FMO II)	847	0
		:	AAC51932.1	flavin containing monooxygenase 3	847	0
: ,			CAA15908.1	dJ127D3.1 (Hepatic Flavin-containing Monooxygenase 3 (Dimethylaniline Monooxygenase (N-Oxide forming) 3, EC1.14.13.8, Dimethylaniline Oxidase 3, FMO IT FMO 3)	1	
			AAH32016.1	flavin containing monooxygenase 3	847	0
·			NP_008825.2	flavin containing monooxygenase 3; Flavin-containing monooxygenase-3	846	C
			S51130	dimethylaniline monooxygenase (N-oxide-forming) (BC 1.14.13.8) 3	846	0
			CAA87632.1	flavin-containing monooxygenase 3 (FMO3)	846	0
		:	A38228	dimethylaniline monooxygenase (N-oxide-forming) (EC 1.14.13.8), hepatic 2	795	0
•		· .	AAA86284.1	flavoprotein	795	0
			CAA15909.1	dJ127D3.2 (Flavin-containing Monooxygenase family protein)	770	0
•		• • • •		FMO2_HUMAN Dimethylamline monooxygenase [N-oxide forming] 2 (Pulmonary flavin-containing monooxygenase 2) (FMO 2) (Dimethylamline oxidase 2) (FMO		
1			. 810867	181)	610	e-174
•			NP 002012.1	flavin containing monooxygenase 1; Flavin-containing monooxygenase 1 (fetal liver)	580	· e-165
"  . "		• :	001740	FMO1_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE FORMING] 1 (FETAL HEPATIC FLAVIN-CONTAINING MONOOXYGENASE 1) (FMO 1) (DIMETHYLANILINE OXIDASE 1)	900	
	1	1:		dimethylaniline monooxygenase (N-oxide-forming) (FC 1 14 13 8) hengic 1	287	6 165
			127.1	flavin-containing monooxygenase	8,5	165
	ı				. 300	-100

	: ,		NP_001451.1	flavin containing monooxygenase 2; Flavin-containing monooxygenase 2 (adult liver)	561	e-159
			CAA70462.1	flavin-containing monooxygenase 2	561	e-159
			CAA15910.1	dJ127D3.3 (Flavin-containing Monooxygenase 2)	561	e-159
			AAH05894.1	flavin containing monooxygenase 2	561	e-159
				FMO5_HUMAN DIMETHYLANILINE MONOOXYGENASE [N-OXIDE FORMING] 5 (HEPATIC FLAVIN-CONTAINING MONOOXYGENASE 5) (FMO		
			P49326	5) (DIMETHYLANILINB OXIDASE 5)	546	e-155
			S71618 ···	dimethylaniline monooxygenase (N-oxide-forming) (BC 1.14.13.8) FMO5	546	e-155
		•	AA:A67849.1	flavin-containing monooxygenase 5	546	e-155
	. :		NP_001452.1	flavin containing monooxygenase 5	545	e-155
	: :		S51131	flavin-containing monooxygenase 5 (FMO5)	. 545	e-155
		1	CAA87633.1.	flavin-containing monooxygenase 5 (FMO5)	. 545	e-155
NM_011012- NP_035142.1	Mm.2991	U:(C-IR) 2.14	NP_000904.1	opiate receptor-like 1; opioid receptor-like 1; kappa3-related opioid receptor	573	e-163
	i	: .	P41146	OPRX_HUMAN Nociceptin receptor (Orphanin FQ receptor) (Kappa-type 3 opioid receptor) (KOR-3)	573	e-163
			S43087 ·	orphan opioid receptor ORL1	573	e-163
	**	·:	CAA54386.1	ORL1	573	e-163
		; .	AAA84913.1	orphan opioid receptor	573	e-163
• .		· ;	AAK11714.1	AF348323_1 nociceptin receptor	573	e-163
		·	AAH38433.1	opiate receptor-like 1	573	e-163
	:		AAL:54890.1	AF126470_1 KOR-3D	558	e-159
	[		AAA96251.1	opioid receptor-like protein	509	e-144
i			2201468A·	opioid orphan receptor	509	e-144
ζ·			CAC17003.1	dJ1022E24.1 (opiate receptor-like protein 1 (OPRL1))	445	e-125
		.:	CAC15482.1	dJ366F13.1 (opioid receptor mu 1)	296	4e-80
		•	P35372	OPRM_HUMAN Mu-type opioid receptor (MOR-1)	296	46-80
	:		156553	mu opiate receptor	296	4e-80
		:	AAA73958.1	opioid receptor	296	4e-80

			2108340A	rm onioid recentor	200	
		<u> </u> :	NP 000905.1	opioid receptor, mu 1.	267	4-80
	. <u> </u>		AAA20580.1	Mu opiate recentor	067	46-90
			565693	Onioid recentor ans consistent MOD 1 A	067	46-80
			7,1200	Protection and Validate MOKIA	293	4e-79
			AAB60354.1	mu opioid receptor variant	293	4e-79
):			AAN87342.1	DRG kappa 1 splice variant KOR 1A	285	8e-77
			P41143	OPRD_HUMAN Delta-type opioid receptor (DOR-1)	285	18-76
	٠.		AAA83426.1	delta opiate receptor	285	10.76
			CAA15671.1	d/212P9,1	284	10.76
NM_015750 NP_056565.1	Mm,4567 o	U.(C-IR) 2.14	NP_005374.1	sialidase 2; cytosolic sialidase; N-acetyl-alpha-neuraminidase 2; neuraminidase 2	539	
i			Q9Y3R4	NER2_HUMAN Sialidase 2 (Cytosolic sialidase) (N-acetyl-alpha-neuraminidase 2)	530	6-153
		. ;	CAB41449.1	neuraminidase; sialidase	530	e-153
			NP_006647.2	sialidase 3; neuraminidase 3; ganglioside sialidase; N-acetyl-alpha-neuraminidase 3	267	46-71
			CAB96131.1	Nuraminidase	. 267	4e-71
	4. 4. 2.		Q9UQ49	NER3_HUMAN Sialidase 3 (Membrane sialidase) (Ganglioside sialidase) (N-acetyl-alpha-neuraminidase 3)	264	3e-70
		1	BAA82611.1	ganglioside sialidase	264	3e-70
	:::	 	CAC81904.1	sialidase	231	2e-60
			NP_542779.2	sialidase	231	36-60
NM_031389 NP_113566.1	Mm.8479 2	U:(C-IR) 2.14	XP_085972.4	similar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	758	0
	10 10 10 10 10		NP_604393.1	PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	758	0
			Q96MN2	NAIA HUMAN NACHT-, LRR- and PYD-containing protein 4 (PAAD and NACHT-containing protein 2) (PYRIN-containing APAF1-like protein 4) (Ribonuclease inhibitor 2)	758	0
	•.•	.\ .\	AAL35293.1	AF442488_1 NALP4	758	0
	· ·	;	AAL68396.1	PAAD and NACHT-containing protein 2	758	C
					1	,

						:
			AAL87104.1	AF479747_1 PYRIN-containing APAF1-like protein 4	758	
	.i		BAB71254.1	unnamed protein product	758	
	: .	-	AAL88672.1	AF482706_1 ribonuclease inhibitor 2	749	10
	1	:	XP_062261.4	similar to PYRIN-containing APAF1-like Protein 7	495	e-130
			NP_659444.1	PYRIN-containing APAF1-like protein 6	427	e-119
		:	P59045	PYA6_HUMAN PYRIN-containing APAF1-like protein 6	427	e-119
		•	AAM14632.1	PYRIN-containing APAF1-like protein 6	427	e-119
· ,	;;	:	AAH34730.1	PYRIN-containing APAF1-like protein 6	427	P-110
		•	AAH16443.1	AAH16443 Unknown (protein for IMAGE:3448931)	30	108
			AAL78632.1	AF468522_1 NALP3 long isoform	379	P-104
1			NP_004886.2	cold autoinflammatory syndrome 1; chromosome 1 open reading frame 7.	378	101
				angiotensin/vasopressin receptor AII/AVP-like; cryopyrin; PYRIN-containing APAF1-like protein 1		
· ·			Q96P20	CIS1_HUMAN Cold autoinflammatory syndrome 1 protein (Cryopyrin) (NACHT-, LRR-and PYD-containing protein 3) (PYRIN-containing APAF1-like protein 1) (Angiotensin/vasopressin recentor AII/AVP-like)	. 378	e-104
			AAL33908.1	AF410477_1 cryopyrin	378	e-104
		·	AAL12497.1	cryopyrin	378	e-104
;	·		AAL65136.1	AF420469_1 PYRIN-containing APAF1-like protein 1	378	e-104
			XP_064988.5	similar to PYRIN-containing APAF1-like protein 4; PAAD and NACHT-containing protein 2; ribonuclease inhibitor 2	367	e-101
NM_025621 NP_079897.1	Mm.1442 59	U:(C:R) 2.11	XP_088993.1	similar to RIKEN cDNA 2310050C09	229	5e-60
3	•					
NM_011377 NP_035507.1	Mm.4775	U:(C-IR) 2.09	NP_005060.1	single-minded (Drosophila) homolog 2 long isoform; human transcription factor SIM2, homolog of the Drosophila single-minded gene SIM1	939	0
			Q14190	SIM2_HUMAN Single-minded homolog 2	939	0
	,		AAB62396.1	transcription factor SIM2 long form	939	0
	<i>:</i>		BAA89433.1	single-minded 2 protein	939	0
•						

			NP_033664.1	single-minded (Drosophila) homolog 2 short isoform; human transcription factor. SIM2, homolog of the Drosophila single-minded oene SIM1	849	0
			AAB62397.1	transcription factor SIM2 short form	840	
			CAA05055.1	human SIM2	77.0	
		· .	NP_005059.2	single-minded (Drosophila) homolog 1; Single-minded, drosophila, homolog of. 1	12.59	0
			P81133	SIM1_HUMAN Single-minded homolog 1	63	180
			AAB62395.1	hSIM1	069	180
			A58520	single-minded gene 2 protein	670	0-100
	}'		BAA12919.1	Sim	461	P-120
			NP 071406.1	basic-helix-loop-helix-PAS protein	205	30 70
		; ,	AAG35180:1	AF164438_1 basic-helix-loop-helix-PAS protein	205	36.70
1	· .		BAB21221.1	NPAS3 (MOP6)	200	57-75 F. 70
	: : :		BAC53756.1	NPAS3	263	36-19
AF319951		TI-(C.R.)			295	Se-79
AAL37178.1	Mm.35253 2.08	2.08	AAM73657.1	solute carrier family 12 member 8	1011	, c
	. "		AAK94307.1	solute carrier family 12 member 8	766	s   ¢
			AAH20506.1	hypothetical protein FLJ23188	370	100
i			NP 078904.1	solute carrier family 12 (potassium/chloride transporters), member 8; solute carrier family 12 (sodium/potassium/chloride transporters) member 8	260	701-0
		:	BAB15571.1	unnamed protein product	369	6-101
		. :	NP 001037.1	solute carrier family 12 (sodium/potassium/chloride transporters), member 2; Solute carrier family 12 (sodium/potassium/chloride transporters)	6	
			P55011	S122_HUMAN Solute carrier family 12 member 2 (Bumetanide-sensitive	227	26.50
· · ·	•		A57187	bumetanide-sensitive Na-K-CI cotransporter	220	26.50
	ant.		AAC50561.1	bumetanide-sensitive Na-K-Cl cotransporter	229	26-59
				Similar to solute carrier family 12 (sodium/potassium/chloride	229	2e-59
		· · · · · · · · · · · · · · · · · · ·	NP_000329.1	sodium potassium chloride cotransporter 2; Solute carrier family 12	. 223	1e-57
, ,		· .	Q13621	S121_HUMAN Solute carrier family 12 member 1 (Bumetanide-sensitive	. 223	1e-57
•			AAB07364.1	burnetanide-sensitive Na-K-2Cl cotransporter	223	1e-57
	•	:				

			,			
			P55017	S123_HUMAN Solute carrier family 12 member 3 (Thiazide-sensitive sodium-chloride	201	40.51
			NP_000330.1	solute carrier family 12 (sodium/chloride transporters), member 3; Solute carrier family 12 (sodium/potassium/chloride transporters)	201	10-01
			ÀAC50355.1	thiazide-sensitive Na-Cl	201	46-51
		:	G01202	NaCl electroneutral Thiazide-sensitive cotransporter	201	56-51
	:		CAA62613.1	NaCl electroneutral Thiazide-sensitive cotransporter	201	5p.51
NM_008074				Y		1020
NP_032100.1	Mm.1345	U.(C-IR) 2.08	NP 150092.1	gamma-aminobutyric acid (GABA) A receptor, gamma 3	. 841	C
			AAB39369.1	GABAA receptor garmina 3 subunit	841	0
	 		099928	GAC3_HUMAN Gamma-aminobutyric-acid receptor gamma-3 subunit precursor (GABA(A) receptor)	838	
			AAF99698.1	GABAA receptor gamma 3 subunit	838	0
	•		AAF63215.1	GABAA receptor gamma 3 subunit	836	0
.			AAD50273.1	gamma-aminobutyric acid A receptor gamma 2	588	e-167
:			NP_000807.1	gamma-aminobutyric acid A receptor, gamma 2 precursor	584	e-166
		· · · · · · · · · · · · · · · · · · ·	P18507	GAC2_HUMAN Gamma-aminobutyric-acid receptor gamma-2 subunit precursor (GABA(A) receptor)	584	e-166
	,		S03905	gamma-aminobutyric acid/benzodiazepine receptor gamma-2 chain precursor	. 584	e-166
			CAA33437.1	GABA-A receptor gamma 2 subunit	584	e-166
		•	1506443A	GABAa receptor gamma2	584	e-166
			AAH31087.1	similar to GAMMA-AMINOBUTYRIC-ACID RECEPTOR GAMMA-1 SUBUNIT PRECURSOR (GABA(A) RECEPTOR)	576	e-164
			XP_094080.1	similar to Gamma-aminobutyric-acid receptor gamma-1 subunit precursor (GABA(A) receptor) [Homo sapiens]	576	e-164
			NP_004952.1	gamma-aminobutyric acid (GABA) A receptor, epsilon, isoform 1 precursor	378	6-104
***		Ì	AAB49284.1	GABA-A receptor epsilon subunit	378	e-104
	.,: : 3.,		P78334	GAB_HUMAN Gamma-aminobutyric-acid receptor epsilon subunit precursor (GABA(A) receptor)	378	e-104
2						

	٠.		CAA70904.1	GABA receptor epsilon subunit	378	e-104
		: : (	AAB94645.1	GABA-A receptor epsilon subunit	378	104
	**		CAA70903.1	GABRE	374	-103
NM_010899 NP_035029.1	Mm.1168 02	U:(C-IR) Q13469 2.08	Q1346 <u>9</u>	NFC2_HUMAN Nuclear factor of activated T-cells, cytoplasmic 2 (T cell transcription factor NFAT1) (NFAT pre-existing subunit)(NF-ATp)	1522	0
			AAC50887.1	transcription factor NFAT1 isoform C	1522	0
;			NP_036472.1	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2; nuclear factor of activated T-cells, cytoplasmic 2	1487	0
	·	;	G02326	transcription factor NFAT1 isoform B - human	1487	0
;			AAC50886.1	transcription factor NFAT1 isoform B	1487	0
		• •	CAC00528.1	d1994O24.1 (nuclear factor of activated T-cells, cytoplasmic 2 (isoforms B and C))	835	0
.;			CAB54871.1	dI1009H6.1.2 (nuclear factor of activated T-cells, cytoplasmic 2, isoform C)	649	0
	,		CAC00529.1	dI1009H6.1.1 (nuclear factor of activated T-cells, cytoplasmic 2, isoform B)	615	e-175
			1A02	N Chain N, Structure Of The Dna Binding Domains Of Nfat, Fos And Jun Bound To Dna	267	e-161
 			AAD00451.1.	transcription factor	551	e-156
			095644	NFC1_HUMAN Nuclear factor of activated T-cells, cytoplasmic 1 (NFAT transcription complex cytosolic component) (NF-ATc1) (NF-ATc)	550	e-156
:	,	. :	AAC50869.1	nuclear factor of activated T cells	523	e-148
	.:		NP_006153.2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1; nuclear factor of activated T-cells, cytoplasmic 1	521	e-147
	, ·		AAD00450.1	transcription factor	521	e-147
·. ·.	, :	U:(C-IR)	NP_037504.1	cysteine knot superfamily 1, BMP antagonist 1; gremlin	311	2e-84
NM_011824 NP_035954.1	Mm.3046 5	2.07 U:(C-D) 2.59				
			AAC39725.1	gremlin	311	2e-84
	;		BAA84462.1	gremlin homologue	311	2e-84
·			AAF06677.1	gremlin	311	2e-84
•			AAG23891.1	AF154054 1 DRM	. 311	2e-84

		:	BAC04620.1	unnamed protein product	254	. 3e-67
•	:		BAC04643.1	unnamed protein product	253	. 8e-67
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		:			Ŀ	·
AF193796	Mm.20706	U:(C-IR)		•		
AAL09298.1	2 ·	2.07	XP 006804.2	similar to Homeobox protein Hox-C13 (Hox-3G)		·
			NP 059106.2	homeo box C13; homeobox protein Hox-C13; homeo box 3G	505	e-142
			P31276	HXCD_HUMAN Homeobox protein Hox-C13 (Hox-3G	505	e-142
		: : : : : : : : : : : : : : : : : : : :	AAF73439.1	HOXC13	505	e-142
	.;		AAH02754.1	homeo box C13	505	e-142
	•		AAF67760.1	homeoprotein C13	504	e-142
			BAB14786.1	unnamed protein product	280	7e-75
	.,*	``	P31271	HXAD_HUMAN Homeobox protein Hox-A13	218	4e-56
			AAC50993.1	transcription factor HOXA13	218	4e-56
6 4			NP_000513.2	homeobox protein A13; homeobox protein HOXA13; homeo box 1J; transcription factor HOXA13	218	. 46-56
		: ·:	NP.000514.1	homeo box D13; homeo box 41; homeobox protein Hox-D13	216	. 2e-55
			P35453	HXDD_HUMAN Homeobox protein Hox-D13 (Hox-41)	216	. 2e-55
			AAC51635.1	HOXD13	216	2e-55
:	. :		BAA95352.1	homeobox transcription factor.	216	2e-55
NM_008152		11-(21-2)				·
NP 032178.1	Mm.2840	2.07	XP_007392.1	similar to G protein-coupled receptor 65; T-cell death-associated gene 8	527	e-149
:			AAH35633.1	similar to G protein-coupled receptor	527	e-149
			NP_003599.1	G protein-coupled receptor 65; T-cell death-associated gene 8	521	e-147
	· · ·	,	AAC31794.1	T cell-death associated protein	521	e-147
		: ':	S68207	G protein-coupled receptor 6C.1	196	. 8e-50
		·	AAA79061.1	G protein-coupled receptor	196	8e-50
		·	2124311B	G protein-coupled receptor	196	8e-50

JU.	, 00	237	·						22	20														<u>.</u>	
•	8e-50	8e-50	8e-50	8e-50	8e-50	8e-50	86-50	. 141		e-141	e-141	6-141	e-141	4e-85	:	0		0	0	0	ó	0	0	86-96	7 / >2
	196	196	196	196	196	196	196	7 700	490	499	499	499	. 499	313		693	. 693	. 693	. 693	693	693	693	629	350	222
	G protein-coupled receptor 4	similar to Probable G protein-coupled receptor GPR4 (GPR19)	GPR4_HUMAN Probable G protein-coupled receptor GPR4 (GPR19)	G protein-coupled receptor 4	G protein-coupled receptor	G protein-coupled receptor	G protein-coupled receptor	indoleamine-pyrrole 2,3 dioxygenase; Indoleamine 2,3-dioxygenase; indole 2,3-dioxygenase	1230_HUMAN Indoleamine 2,3-dioxygenase (IDO) (Indoleamine-pyrrole 2,3-dioxygenase)	indoleamine-pyrrole 2,3-dioxygenase (EC 1.13.11.42)	indoleamine 2,3-dioxygenase	indolearnine 2,3-dioxygenase (IDO) (BC 1.13.11.17)	indoleamine-pyrrole 2,3 dioxygenase	similar to indoleamine 2,3-dioxygenase		cholecystokinin A receptor	CCKR_HUMAN Cholecystokinin type A receptor (CCK-A receptor) (CCK-AR)	cholecystokinin type A receptor	cholecystokinin A receptor	cholecystokinin A receptor	cholecystokinin type A receptor	cholecystokinin type-A receptor	cholecystokinin A receptor	GASR_HUMAN Gastrin/cholecystokinin type B receptor (CCK-B receptor) (CCK-BR)	
	NP_005273.1	XP_009140.1	P46093	A57641	AAA98457.1	I53033· .	AAA63180.1	NP_002155.1	P14902	PC1161	CAA35663.1	AAA36081.1.	AAH27882.1	XP 095645.4	•	NP_000721.1	P32238	JN0692	AAA35659.1	AAA02819.1	AAA91123.1	BAA90879.1	2118221A	P32239	
		·			,			U:(C-R) 2.07							U:(C-R)			:		:		7			
					•		·	Mm.392	;		•		-		!	Mm.3521.		:		:	·. :				•
				:				NM_008324 NP_032350.1					•	:	NM_009827	NP 033957.1						1		: .	:

.;						
			A47430	gastrin/cholecystokinin receptor B, short splice form	350	8e-96
	,		ÄAA35660.1	cholecystokinin receptor	350	8e-96
			AAA35657.1	cholecystokinin-B/gastrin receptor	350	8e-96
			AAC37528.1	gastrin receptor	350	8P-96
	.		BAA02564.1	cholecystokinin receptor	350	86.96
-		·	AAH00740.1	AAH00740 cholecystokinin B receptor	350	8e-96
			AAA91831.1	cholecystokinin B receptor	348	28-05
			AAB30766.2	cholecystokinin B receptor	348	20.05
	:	·	BAA:04759.1	cholecystokinin-B receptor/gastrin receptor	348	Ap 05
,		. :	AAC27510.1	osetrin)cholemetolinin hanin segmetes	07.0	#C-22
	·.		AAK38351.1	CCK_Bloschin recentor weight	345	3e-94
			AAN32829	AR41170 1 cholometalinin Canada	243	221 EQ
		-	NTD 000727.7	The care of the ca	243	1e-63
			INF 000/22.2	cholecystokunn B receptor	. 241	. 5e-63
			AAF67174.1	AF239668_1 CCK-B/gastrin receptor	241	5e-63
NM_013920 NP_038948.1	Mm.4198 5	U:(C-IR) 2.07	JC6095	hepatocyte nuclear factor 4 gamma chain	749	0
			2208436B	hepatocyte nuclear factor 4	740	
:		٠	NP_004124.2	hepatocyte nuclear factor 4, gamma	730	
	•		1	hepatocyte nuclear factor 4 gamma (HNF4gamma)	720	
		1, 3, 4, 2, 3	Q14541	HN4G HUMAN Hepatocyte nuclear factor 4-gamma (HNF-4-gamma)	738	5
			AAF00110.1	hepatocyte nuclear factor 4 gamma	738	7
			CAA61133.1	Hepatocyte nuclear factor 4A	582	P-166
	. :	· · · · · · · · · · · · · · · · · · ·	AAB48082.1	hepatocyte nuclear factor 4-alpha	570	9-165
		:	NP_000448.2	hepatocyte nuclear factor 4, alpha; transcription factor-14; hepatic nuclear factor 4, alpha	579	e-165
			JC6096	hepatocyte nuclear factor 4 alpha2 chain	579	P.165
*			CAA89989.1	hepatocyte nuclear factor 4 alpha (HNF4alpha4)	579	e-165
		1	2208436A	hepatocyte nuclear factor 4:ISOTYPE=alpha	579	e-165
	· · :					

			١,	2 7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		
			20.5	d/1013A22.1 (hepatocyte nuclear factor 4, alpha)	578	e-165
			P41235	HN4A_HUMAN Hepatocyte nuclear factor 4-alpha (HNF-4-alpha) (Transcription factor HNF-4) (Transcription factor 14)	578	e-165
	  		CAA54248.1	hepatocyte nuclear factor 4	323	0.164
	`\	;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;	JC4937	hepatocyte nuclear factor 4, splice form B	575	6-164
			CAA61134.1	Hepatocyte nuclear factor 4B	X. X.	164
NM_020028 NP_064412.1	Mm.2325	U.(C.IR) 2.07	NP_004711.2	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4; G protein-coupled receptor; lysophosphatidic acid receptor BDG4: 1:04	470	6-132
	.!		ОЭНВМО	EDG4_HUMAN Lysophosphatidic acid receptor Edg-4 (LPA receptor 2) (TPA-2)	ATO.	0 120
		:	AAB61528.1	R33799_1	027	6 132
			AAF43409.1	AF233092_1 lysophosphatidic acid G protein-coupled recentor 4	470	6 122
		,	AAH25695.1	endothelial differentiation, lysophosphatidic acid G-protein-coupled recentor 4	470	22
			AAG28521.1	AF197929_1 lysophosphatidic acid receptor BDG4	468	121
		•	AAC27728.1	G protein-coupled receptor Edg-4	463	-130
	:		NP 001392.2		255	20-67
			NP_476500.1	lysophosphatidic acid receptor EDG2; ventricular zone gene 1; LPA receptor EDG2	255	75-67
		•	Q92633	EDG2_HUMAN Lysophosphatidic acid receptor Edg-2 (LPA receptor 1) (LPA-1)	255	2e-67
		·	CAA70686,1	G protein-coupled receptor Bdg-2	255	. 2e-67
		:	AAC00530.1	Edg-2 receptor	255	2e-67
			AAH30615.1	Unknown (protein for MGC:33156)	255	2e-67
			AAH36034.1	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	255	2e-67
		·	JC5293	lysophosphatidic acid receptor	255	2e-67
	•		AAC51139.1	lysophosphatidic acid receptor homolog	255	2e-67
			CAA70687.1	G protein-coupled receptor Edg-2	255	JA.67
		·	NP_036284.1	endothelial cell differentiation gene 7; calcium-mobilizing lysophosphatidic acid receptor LP-A3; LPA receptor BDG7	. 225	36-58
			Q9UBYS	EDG7_HUMAN Lysophosphatidic acid receptor Edg-7 (LPA receptor 3) (LPA-3)	225	36-58
			AAD56311.1	AF127138 1 lysophosphatidic acid G protein-compled recentor	325	2000
			1	Toldman manage a standard of the standard of t	C77	26-08

	2e-65	3e-61	3e-61	3e-61	3e-61	3e-61	e-173	6-173	6 e-173	e-173	24 901-9 t	e-106	t e-106	t e-106	t e-106	t e-106	5 4e-77	6 4e-77	5 9e-77	2 . 96-77	5 9e-77
	248	233	233	233	233	233	909	909	909	605	384	384	384	384	. 384	384	286	286	. 285	. 285	285
	seven transmembrane helix receptor	super conserved receptor expressed in brain 3	SRB3_HUMAN Super conserved receptor expressed in brain 3	G-protein coupled receptor, SREB3	SREB3	AAH09861 super conserved receptor expressed in brain 3	carbonic anhydrase VB, mitochondrial precursor; carbonic dehydratase	CA5B_HUMAN Carbonic anhydrase VB, mitochondrial precursor (Carbonate dehydratase VB) (CA-VB)	carbonic anhydrase VB	carbonic anhydrase VB, mitochondrial	carbonic anhydrase VA, mitochondrial precursor; carbonic anhydrase V, mitochondrial; carbonic dehydratase	CAH5_HUMAN Carbonic anhydrase VA, mitochondrial precursor (Carbonate dehydratase VA) (CA-VA)	carbonate dehydratase (EC 4.2.1.1) V precursor [validated]	carbonic anhydrase V	carbonic anhydrase V; CA V	carbonic anhydrase V	Human Carbonic Anhydrase Ii[hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s)	Human Carbonic Anhydrase Ii[hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Ser (A65s) - Orthorhombic Form	Human Carbonic Anhydrase Ii [hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Thr (A65t)	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N- [(2,3-Difluorophenyl)methyl]-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With
	BAC05911.1	NP_061842.1	99SN6Q	JC7289	BAA96647.1	AAH09861.1	NP_009151.1	Q9Y2D0	BAA76671.1	AAH28142.1	NP_001730.1	P35218	CRHUS	AAA02890.1	AAB47048.1	AAC99806.1	αĐΩι	1066	1UGF	1G52	1654
		:				•	U:(C-IR) 2.05	, .				.:									
		;;,	1.				Mm.1170 15		:									1 .			
.*·\ :					,44 - 5 - 1		NM_019513 NP_062386.1												· · · · ·		

	9e-77	9e-77	9e-77	.9e-77	9e-77	9e-77	225 	9e-77	9e-77	9e-77	1	11:	Ŀ.	9e-77	11:	12	12
	8	96	96	.96	96	8.	86	8	8	8	9e-77	96-77	. 9e-77	96	9e-77	9e-77	9e-77
	285	285	285	285	285	285	285	285	285	285	. 285	285	285	285	285	285	285
	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6629  2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 2-(3-Methoxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-Fluorobenzenesulfonamide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2,6-Difluorophenyl)methyl]-Benzamide.	A Chain A, Carbonic Anhydrase Ii Complexed With (S)-N-(3-Indol-1-YI-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With (R)-N-(3-Indol-1-YI-2-Methyl-Propyl)-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With Al-8520 2h-Thieno[3,2-E]-1,2-Thiazine-6-Sulfonamide, 4-Amino-3,4-Dihydro-2-(3-Methoxypropyl)-, 1,1-Dioxide, ®	A Chain A, Carbonic Anhydrase Ii Complexed With Al-6619 2h-Thieno[3,2-B]-1,2-Thiazine-6-Sulfonamide, 2-(3-Hydroxyphenyl)-3-(4-Morpholinyl)-, 1,1-Dioxide	A Chain A, Carbonic Anhydrase Ii Complexed With 2,6-Diffuorobenzenesulfonamide	A Chain A, Carbonic Anhydrase Ii Complexed With N-[2-(1h-Indol-5-YI)-Butyl]-4-Sulfamoyl-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With 4-(Aminosulfonyl)-N-[(2-Fluorophenyl)methyl]-Benzamide	A Chain A, Carbonic Anhydrase Ii Complexed With 3,5-Difluorobenzenesulfonamide	Catbonic Anhydrase Ii Inhibitor: Acetohydroxamate	A Chain A, The Mechanism Of Cyanamide Hydration Catalyzed By Carbonic Anhydrase Ii Revealed By Cryogenic X-Ray Diffraction	Carbonic Anhydrase Ii Complex With The 10km Inhibitor 4-Sulfonamide-[1-(4-Aminobutane)]benzamide	Carbonic Anhydrase Ii Inhibitor	Carbonic Anhydrase Ii Inhibitor	Carbonic Anhydrase Ii Inhibitor
	118Z	1IF4	1G53	1IF8	1IE7	1190	1191	1IF5	1IF9.	1G1D	1IF6	1AM6	1F2W	10KM	1BN1.	1BN4	IBN3
				:										1			
-				.1 .	,						1 1				;		
								:									

:	:		1BNV	Carbonic Anhydrase Ii Inhibitor	285	00 77	
		:	1BNM.	Carbonic Anhydrase Ii Inhibitor	28,5	00 77	
:			1CIL	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complexed With The Inhibitor Fre	305	77-26	
:: ·	٠		2CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) Complex With Thiocyanate Ion	285	96-77	
:		·.	3CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (E.C.4.2.1.1) Complex With 3-Mercuri 4-Aminohemenifonamida (AMC)	285	9e-77	
:		: 4	1CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (R C 4 2 1 1)	200	. 00 777	
	:		IBNT	Carbonic Anhydrase Ii Inhibitor	285	00-77	
			IBNU	Carbonic Anhydrase Ii Inhibitor	285	9e-77	
			1A42	Human Carbonic Anhydrase Ii Complexed With Brinzolamide	285	96-77	
	·		1BNW	Carbonic Anhydrase Ii Inhibitor	· 285	96-77	_22
			1BNQ	Carbonic Anhydrase Ii Inhibitor	. 285	96-77	26
	; ;		10KN	Carbonic Anhydrase Ii Complex With The 1okn Inhibitor 4-Sulfonamide-[1-(4-N-(5-Fluorescein Thiourea)butane)]	285	9e-77	
			10KL	Carbonic Anhydrase Ii Complex With The 10kl Inhibitor 5-Dimethylamino-Naphthalene-1-Sulfonamide	285	96-77	
			1CRA	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complex With 1,2,4-Triazole	285	9e-77	
			1CAO	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complex With Hydrogen Sulfide	285	9e-77	
			2CBA	Carbonic Anhydrase Ii (B.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, Ph 7.8)	285	9e-77	
		.: :	2CBD	Carbonic Anhydrase Ii (E.C.4.2.1.1) (2.4 M Ammonium Sulfate, 0.3 M Sodium Bisulfite, Ph 7.3)	285	77-96	
			2СВВ	Carbonic Anhydrase Ii (B.C.4.2.1.1) (80 Mm Sodium Citrate, 2.4 M Ammonium Sulfate, Ph 6.0)	285	9e-77	
*			1RAY	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complex With Azide	285	9e-77	
	· · · · · · · · · · · · · · · · · · ·		1RZB	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By By Cobalt(II) At Ph 6.0	285	9e-77	
	- A 1		2CBE	Carbonic Anhydrase Ii (B.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 2mm Dipicolinate, Ph 7.8)	285	9e-77	
, , , , , , , , , , , , , , , , , , ,		.1:3	2CBC	Carbonic Anhydrase Ii (B.C.4.2.1.1) (50 Mm Tris, 3 M Ammonium Sulfate, 0.2 Formate, Ph 7.6)	285	9e-77	
					_		

		1САН	Carbonic Anhydrase Ii (E.C.4.2.1.1) (Native Zinc Replaced By Cobalt) Complex With	285	72-96
	_	1RZC	Carbonic Anhydrase Ii (B.C.4.2.1.1) With Zinc Replaced By Connerffi)	285	77
	_	1BCD	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complex With Trifluoromethane Sulphonamide	285	
	_	1RAZ	Carbonic Anhydrase Ii (B.C.4.2.1.1) Complex With Bromide	285	
		1RZA	Carbonic Anhydrase Ii (B.C.4.2.1.1) With Zinc Replaced By Cobalt(Ii)	285	
		IRZD	Carbonic Anhydrase Ii (E.C.4.2.1.1) With Zinc Replaced By Manganese(Ii)	285	
>	_	1RZE	Carbonic Anhydrase Ii (B.C.4.2.1.1) With Zinc Replaced By Nickel(Ii)	285	
		1CAY-	Carbonic Anhydrase Ii (E.C.4.2.1.1) Complex With Acetate	285	
.:		SCAC .	Carbonic Anhydrase Form C (E.C.4.2.1.1) Complex With Hydrogen Sulfite	285	1.
·		4CAC	Carbonic Anhydrase Form C (B.C.4.2.1.1) (Ph 6)	285	
,	_	1BV3	A Chain A, Human Carbonic Anhydrase Ii Complexed With Urea	285	
		1AVN · · ·	Human Carbonic Anhydrase Ii Complexed With The Histamine Activator	285	9e-77
		1LZV	A Chain A, Site-Specific Mutant (Tyr7 Replaced With His) Of Human Carbonic Anhydrase Ii	285	96-77
l		NP_000058.1	carbonic anhydrase II; carbonate dehydratase II; carbonic dehydratase; carbonic anhydrase B	· 285	96-77
	124	P00918	CAH2_HUMAN Carbonic anhydrase II (Carbonate dehydratase II) (CA-II) (Carbonic anhydrase C)	285	9e-77
•	$\subseteq$	CRHU2	carbonate dehydratase (BC 4.2.1.1) II [validated]	285	9e-77
:		1EOU	A Chain A, Crystal Structure Of Human Carbonic Anhydrase Ii Complexed With An Anticonvulsant Sugar Sulfamate	285	9e-77
		1CNX	Mol_id: 1; Molecule: Carbonic Anhydrase Ii; Chain: Null; Synonym: Carbonate Dehydratase, Hca Ii; Ec: 4.2.1.1; Heterogen: Benzenesulfonamide	. 285	<i>LL</i> -96.
		1CNW	Mol_id: 1; Molecule: Carbonic Anhydrase Ii; Chain: Null; Synonym: Carbonate Dehydratase, Hca Ii; Ec: 4.2.1.1; Heterogen: Bthylaminocarbonylbenzenesulfonamide	285	9e-77
		1CNY	Mol_id: 1; Molecule: Carbonic Anhydrase Ii; Chain: Null; Synonym: Carbonate Dehydratase, Hca Ii; Ec: 4.2.1.1; Heferogen: Aminocarbonylbenzenesulfonamide	285	9e-77
•		4CA2	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (B.C.4.2.1.1)	285	9e-77
		1CA3	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (B.C.4.2.1.1) (pH 5.7)	285	9e-77

:			1HCA ·	Carbonic Anhydrase II (Carbonate Dehydratase) (HCA II) (B.C.4.2.1.1) (pH 6.5)	285	9e-77
:			CAA68426.1	carbonic anhydrase II (AA 1-260)	285	9e-77
	• :		AAA51908.1	carbonic anhydrase II	285	9e-77
• • •	:		AAA51909.1	carbonic anhydrase II	285	9e-77
	.:		ÄÄA51911.1:	carbonic anhydrase II	285	9e-77
	· · ·		1UGB	Human Carbonic Anhydrase Ii[hcaii] (B.C.4.2.1.1) Mutant With Ala 65 Replaced By Gly (A65g)	285	1e-76
			1LG5	A Chain A, Crystal Structure Analysis Of The Hea Ii Mutant T199p In Complex With Beta-Mercaptoethanol	285	1e-76
			11.G6	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Thiocyanate	285	1e-76
			1LGD	A Chain A, Crystal Structure Analysis Of Hca Ii Mutant T199p In Complex With Bicarbonate	285	1e-76
NM_008890		U:(C-IR)				
NP 032916.1	Mm.57030 2.04	2.04	NP_002677.1	phenylethanolamine N-methyltransferase	462	e-130
			P11086	PNMT_HUMAN Phenylethanolamine N-methyltransferase (PNMTase) (Noradrenaline N-methyltransferase)	462	e-130
·			A28171	phenylethanolamine N-methyltransferase (EC 2.1.1.28)	462	e-130
		:	1HNN	B Chain B, Crystal Structure Of Human Pmnt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
:		. :	1HNN	A Chain A, Crystal Structure Of Human Pnmt Complexed With Sk&f 29661 And Adohcy(Sah)	462	e-130
. ; ,! :			AAA60130.1	phenylethanolamine N-methyltransferase	462	e-130
		,	CAA36944.1	phenylethanolamine n-methyltransferase	462	e-130
	,	:	AAH37246.1	phenylethanolamine N-methyltransferase	462	e-130
	٠:٠	:	ÀÀA60131.1	phenylethanolamine N-methyltransferase	461	e-130
NM_008985 NP_033011.1	Min.2902	U:(C-IR) 2.04	NP 002837.1	protein tyrosine phosphatase, receptor type, N precursor; islet cell antigen 2; islet cell antigen 512; islet cell autoantigen 3; protein tyrosine phosphatase-like N precursor	1389	0

	:		Q16849	PTPN_HUMAN Protein-tyrosine phosphatase-like N precursor (R-PTP-N) (PTP IA-2)(Islet cell antigen 512) (ICA 512) (Islet cell autoantigen 3)	1380	
			AAA90974.1	tyrosine phosphatase .	1380	0
;			CAA44688.2	Islet Cell Antigen 512	972	
			AAH07713.1	AAH07713 protein tyrosine phosphatase, receptor type, N	972	0
:			137577	islet cell antigen 512	850	0
			 NP_570857.1	protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 2 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatas		
			AAB68603.1	protein tyrosine phosphatase receptor pi	607	e-173
		, [.]	NP 002838.1	protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 1 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	209	6-173
1,		:	092932	PTPX_HUMAN Protein-tyrosine phosphatase X precursor (R-PTP-X) (Islet cell autoantigen related protein) (ICAAR) (IAR) (Phogrin)	. 607	
	· · · · · · · · · · · · · · · · · · ·		JC5062	phogrin precursor	209	e-173
			742.1	phogri	. 607	e-173
			JC5263	transmembrane tyrosine phosphatase-like protein, ICAAR	209	· e-173
				Islet Cell Autoantigen Releted	. 607	e-173
				IAR/receptor-like protein-tyrosine phosphatase precursor	209	e-173
			BAA20841.2	KIAA0387	. 607	e-173
			NP_570858.1	protein tyrosine phosphatase, receptor type, N polypeptide 2, isoform 3 precursor; protein tyrosine phosphatase receptor pi; phogrin; tyrosine phosphatase IA-2 beta; IAR/receptor-like protein-tyrosine phosphatase	025	164
	1		AAH34040.1	protein tyrosine phosphatase, receptor type, N polypeptide 2	579	e-164
	,	U.(C-IR) 2.03	AAK74066.1	odd-skipped-related 2A protein	481	e-152
NM_054049 NP_473390.1	Mm.4633 6	U:(C-R) 2.46			• • •	
			BAC11035.1	unnamed protein product	484	e-152
			AAH16936.1	AAH16936 odd-skipped-related 2A protein	509	e-144
	.•	•				

			NP_443727.1	odd-skipped-related 2A protein	507	e-143
•	,	·	AAK74067.1	odd-skipped-related 2B protein	507	e-143
	, ; ; ;		XP_059439.2	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	2e-95
			NP_660303.1	similar to odd-skipped related 1 (Drosophila); odd-skipped related gene; odz (odd Oz/ten-m) homolog (Drosophila) related 1	347	. 2e-95
· · · · · · · · · · · · · · · · · · ·			AAH25712.1	Similar to odd-skipped related 1 (Drosophila)	347	2e-95
			BAB92079.1	zinc finger transcription factor	347	2e-95
			BAC11079.1	unnamed protein product	347	2e-95
NM_007924		(ar 2)-11				
NP 031950.1	Mm.1552	2.03	NP_006523.1	ELL gene (11-19 lysine-rich leukemia gene)	880	0
			P55199	BLL_HUMAN RNA polymerase II elongation factor ELL (Eleven-nineteen lysine-rich leukemia protein)	088	230
		·. :	I38880 · ·	eleven-nineteen lysine-rich leukemia gene (BLL) protein	880	0
. \			AAA57120.1	BLL	880	0
· '*:	:		AAB34056.1	MEN chimeric transcription factor	803	0
	;	•	NP_036213.1	ELL-related RNA polymerase II, elongation factor	371	e-102
	·	•	000472	ELL2_HUMAN RNA polymerase II elongation factor ELL2	371	e-102
			AAC51232.1	RNA polymerase II elongation factor ELL2	371	e-102
	:		AAH28412.1	ELL-RELATED RNA POLYMERASE II, ELONGATION FACTOR	371	e-102
NM_008521		(ar 2)11				
NP 032547,1	Mm.4088	2,03	AAH29498,1	Jeukotriene C4 synthase	704	56-53
÷	;; ;; ;;		JC5398.	leukotriene C4 synthase (EC 6)	204	7e-53
			NP_665874.1	leukotriene C4 synthase isoform 1	204	7e-53
. 1	:.		Q16873	LC4S_HUMAN Leukotriene C4 synthase (Leukotriene-C(4) synthase) (LTC4 synthase)	204	76-53
· :			I38595 · · ·	leukotriene-C4 synthase (EC 2.5.1.37)	204	7e-53
	· .	:	AAA20467.1	leukotriene C4 synthase	204	70-53

00:	5/08	323	98					_			23	ı							US.	200.		,		
	. 7e-53	7e-53	7e-53	96-95	96-95	96-95	96-95	96-95	96-95	2e-91	23	2e-91	1e-90	e-148		e-148	e-148	e-146	4e-87	26-84		5	c	,
	204	204	204	. 345	. 345	345	345	345	345	333	333	333	331	522	3	277	222	445	319	310	000	066	066	
	Leukotnene-C4 synthase	leukotriene C4 synthase	leukotriene C4 synthase	chymase 1, mast cell preproprotein; chymase, mast cell; chymase, heart; mast cell protease I	MCT1_HUMAN Chymase precursor (Mast cell protease I)	chymase (BC 3.4.21.39) precursor [validated]	chymase	mast cell chymase	chymase	Crystal Structure Of Pmsf-Treated Human Chymase At 1.9 Angstroms Resolution	chymase	chymase	A Chain A, The 2.2 A Crystal Structure Of Human Chymase In Complex With Succinyl-Ala-Ala-Pro-Phe-Chloromethylketone	ring finger protein 32	himothetical protein	AR325600 1 BESC33	AF441222 1 ring finger protein RME22	AC005534_2 supported by human ESTs AA412402 (NID:g2070990) NH44021 (NID:g1182549), mouse EST AA065933 (NID:g1562789), and genscan	AAH15416 Similar to hypothetical protein DKFZp434C135	Similar to ring finger protein 32	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1; ecotropic retroviral receptor; Solute carrier family 7 (cationic amino acid transporter, y+ system), amino acid transporter,	CTR1_HUMAN High-affinity cationic amino acid transporter-1 (CAT-1) (CAT1)	(System Y+ basic amino acid transporter) (Ecotropic retroviral leukemia receptor homolog) (ERR) (Ecotropic retrovirus receptor homolog)	
A A A COPPE 4	AAASUSSS.I	AAC50476.1	AAB06723.1	NP_001827.1	P23946	KYHUCM .	AAA52019.1	AAA52020.1	AAA52021.1	1KLT	AAB26828.1	1914144A	1PJP	NP_112198.1	CAR66808 1	A A G-50281 1	AAM18664.1	AAD43189.1	AAH15416.1	AAH28120.1	1 9E0303 dN		P30825	
				U:(C-IR) 2.03		٠				1	. •	·		U:(C-IR) 2.03							· U.(C-IR) 2.02		,	•
				Mm.1252			• • •							Mm.8735						·	Mm.5255			
				NM_010780 -NP_034910.1					::					NM 021470 NP 067445.1				, , , , , , , , , , , , , , , , , , ,		:	NM_007513 NP 031539.1	:		

			CAA41869.1	retroviral receptor	000	
	-·.		AAC27721.1	cationic amino acid transporter	066	
•			S29685	refravired resemble	066	0
			200000	renovina receptor	988	0 .
			CAA40560.1	RECIL	. 988	0
			P52569	CIR2_HUMAN Low-affinity cationic amino acid transporter-2 (CAT-2) (CAT2)	654	0
			BAA06271.1	cationic amino acid transporter 2	654	0
. , ,	•		NP 003037.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2; Solute carrier family 7 (cationic amino acid transporter, y+ system),; amino acid transporter, cationic 2		
			AAB62810.1	hCAT-2A	0 to	) 6
<i>:</i> .			NP 116192.2	solute carrier family 7 (cationic amino acid transporter, v+ system). member 3	640	
		;	AAL37184.1	cationic amino acid transporter	640	23
·	. ,		BAC11353.1	unnamed protein product	640	52 C
1.		·	AAH33816.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 3	639	0
	·		BAC11253.1	unnamed protein product	637	C
		:	BAB55118.1	unnamed protein product	421	e-117
:			XP_036892.1	similar to Cationic amino acid transporter-4 (CAT-4) (CAT4)	411	e-114
			AAH08814.1	Unknown (protein for MGC:10733)	. 411	e-114
			NP 004164.1	solute carrier family 7 (cationic amino acid transporter, v+ system). member 4	. 393	e-100
			043246 · · ·	CTR4_HUMAN Cationic amino acid transporter-4 (CAT-4) (CAT4)	. 393	e-109
	· .		CAA04263.1	cationic amino acid transporter 3	393	e-109
NM_007962	•		· .			
NP 031988.1	Mm.33240 2.02	U:(C-IR) 2.02	NP_005788.1	epithelial V-like antigen 1 precursor	330	38-00
			NP_658911.1	epithelial V-like antigen 1 precursor	330	36-90
			060487	EVA1_HUMAN Epithelial V-like antigen 1 precursor	330	36-90
			AAC39762.1	epithelial V-like antigen precursor	330	36-90
.:		÷.	AAF87240.1	AF275945_1 epithelial V-like antigen 1	330	36-90
			AAG23183.1	AF304447 1 epithelial V-like antigen 1	330	36-90
	•				) )	ころうつ

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30.00	e-117	6 117	C-117	0 117	P-117	6.117	e-117	6-117	e-117	e-117	· e-117	e-117	e-116	e-116	e-116	e-116	e-115	e-115	e-115		e-115	e-115	e-115	0	
330	420	420	420	420	420	420	418	418	418	418	418	418	416	416	415	414	413	412	412		412	412	412	1821	
epithelial V-like antigen 1	1B05_HUMAN HLA class I histocompatibility antigen, B-13 B*1301 alpha chain precursor (B13.1)	MHC class I histocompatibility antigen HLA-B13 precursor	MHC HLA-B13 precursor	MHC HLA-B13 chain	HLA-B*1302 antigen	MHC class I antigen	MHC class I antigen	MHC class I histocompatibility antigen HLA-B13.1	HLA-B13 protein	HLA-B*1301 antigen	glycosylation aa 86, alpha domain 1 aa 1-24, alpha domain 2 aa 25-114, alpha domain 3 aa 207-298	MHC class I antigen	MHC class I lymphocyte antigen	HLA-B38	MHC antigen	MHC class I antigen HLA-B precursor	lymphocyte antigen	HLA class I antigen HLA-B	1B32_HUMAN HLA class I histocompatibility antigen, B-39 B*3902 alpha chain	precursor (B39.2)	MHC class I instocompatibility antigen precursor	lymphocyte antigen	MHC class I antigen	GLI-Kruppel family member GLI2 isoform beta; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-resnonsive element 25 km semmon 1: 4:	tax-responsive element-2 holding protein
AAH17774.1	P30461	154442	AAA52657.1	AAA59660.1	BAA08822.1	CACI7136.1	CAC17137.1	A45850	AAA59627.1	BAA08821.1	AAA59618.1	CAC29063.1	AAÄ73509.1	AAD00010:1	AAB06829.1	AAA98506.1	184488	AAC31793.1	P30476	150050	000001	AAA52659.1	AAA87396.1	NP_084656.1	
	U:(C-IR) 2.02	:			:-	<u> </u>				:				:								• . ]		U:(C-IR) 2.02	
	Mm.1960 32					· •		÷			•	•	•	; : : :	• :				. `					Mm.1976	
	NM_010393 NP_034523.1										,				1.	5 5									X99104

rotein; 1263 rotein; 1263 r 1252 nding 1252 nc 1043 nc 1004 1004 1004 1004 730 730 7445 ogene 445	
xrotein:  nding  nc  nc  nc  nc  nc  nc  nc  nc  nc	oteini ot
GLI-Kruppel family member GLIZ isoform delta; oncogene GLIZ; tax helper p 2; zinc finger protein GLIZ; tax-responsive element-25-bp sequence binding pt tax-responsive element-2 holding protein hGLIZ  GLI-Kruppel family member GLIZ isoform gamma; oncogene GLIZ; tax helpe protein 2; zinc finger protein GLIZ; tax-responsive element-25-bp sequence bit protein; tax-responsive element-2 holding protein  hGLIZ  GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zin finger protein GLI3  GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zin finger protein  GLI3 protein  GLI3 HUMAN Zinc finger protein GLI3  DNA-binding protein  Tax helper protein 1  Tax helper protein 2  glioma-associated oncogene homolog  GLI1 HUMAN Zinc finger protein GLI1 (Glioma-associated oncogene) (Oncogli)	GLI-Kruppel family member GLI2 isoform delta; oncogene GLI2; tax helper protein; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein  hGLI2 GLI-Kruppel family member GLI2 isoform gamma; oncogene GLI2; tax helper protein 2; zinc finger protein GLI2; tax-responsive element-25-bp sequence binding protein; tax-responsive element-2 holding protein  hGLI2 GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zinc finger protein GLI3  GLI-Kruppel family member GLI3; oncogene GLI3; DNA-binding protein; zinc finger protein  GLI3 protein  GLI3 HUMAN Zinc finger protein GLI3  DNA-binding protein 1  Tax helper protein 1  Tax helper protein 2  glioma-associated oncogene homolog  GLI1_HUMAN Zinc finger protein GLI3 (Glioma-associated oncogene) (Oncogene GLI)  transforming protein gli  GLI protein (AA 1-1106)
BAA25668.1 hGLI2 NP_084657.1 GLI-Kruppel family member GLI2 isoform gamma; on protein 2; zinc finger protein GLI2; tax-responsive element-2 holding protein protein; tax-responsive element-2 holding protein BAA25667.1 hGLI2 NP_000159.2 GLI-Kruppel family member GLI3; oncogene GLI3; D finger protein GLI3 CAB59315.1 GLI3 protein P10071 GLI3 protein P10071 GLI3 HUMAN Zinc finger protein GLI3 AA5227 190K DNA-binding protein GLI3 BAA03568.1 Tax helper protein 1 BAA03569.1 Tax helper protein 2 NP_005260.1 glioma-associated oncogene homolog P08151 GLI1_HUMAN Zinc finger protein GLI1 (Glioma-associated OLI3)	
:	

1		,				
		ひ(C-民)	BAA19667.1	Similar to Rat growth factor Arc (U19866)	765	0
NM_018790 NP_061260.1	Mm.2540 5	U:(C-D) 2.34	ì			
٠.			NP_056008.1	activity-regulated cytoskeleton-associated protein	763	6
	:		AAF07185.1	AF193421_1 ARC	763	0
		·	AAG33705.1	AF248637_1 activity-regulated cytoskeleton-associated protein	763	0
		·	AAH12321.1	AAH12321 Similar to activity-regulated cytoskeleton-associated protein	763	0
		U:(C-IR)	NP_066013.1	ррм36.	2055	0
NM_020043 NP_064427.1	Mm.1437 41	2.01 U:(C-D) 2.17				
			BAB86306.1	hDDM36	2055	235
	:		BAB13454.1	KIAA1628 protein	1539	
	·. :		AAC51287.1	neogenin	260	28-68
			NP 002490.1	neogenin homolog 1 (chicken); neogenin (chicken) homolog 1	260	2e-68
			092859	NEO1_HUMAN Neogenin precursor	260	2e-68
	•		AAB17263.1	neogenin	260	2e-68
•		•	NP_005206.1	deleted in colorectal carcinoma.	. 226	2e-58
·			P43146.	DCC_HUMAN Tumor suppressor protein DCC precursor (Colorectal cancer suppressor)	226	2e-58
٠,			A54100	tumor suppressor protein DCC precursor	. 226	. 2e-58
· :		·	CAA53735.1	tumour suppressor	226	2e-58
			AAA35751.1	colorectal tumor suppressor (put.); putative	216	3e-55
	·;	ひ:(C-球)	Q9UP79	ATS8_HUMAN ADAMTS-8 precursor (A disintegrin and metalloproteinase with	1404	0
NM_013906 NP_038934.1	Mm.1005 82	U.(C-D) 2.16		unompospondin monis 8) (ADAM-1S 8) (ADAM-1SS) (METH-2) (MBTH-8)		
		•	AAD48081.1	AF060153_1 METH2 protein	1404	0.
		•	NP 008968.2	a disintegrin and metalloprotease with thrombosnondin motife-8	1402	
•					-127	5

0	0			\ \.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\.\				0	, o	e-15	· e-154					.3e-87			1e-74					
799	799	799	70%	798	798	798	795	733	733	543	543	543	543	426	426	321	279	279	279	266	263	263	262	
a disintegrin and metalloprotease with thrombospondin motifs-1 preproprotein; human metalloproteinase with thrombospondin type 1 motifs	AF207664_1 matrix metalloprotease	metalloprotease with thrombospondin type 1 motifs	AF060152_1 METH1 protein	ATS1_HUMAN ADAMTS-1 precursor (A disintegrin and metalloproteinase with thrombospondin motifs 1) (ADAM-TS 1) (ADAM-TS1) (METH-1)	AF170084_1 metalloproteinase with thrombospondin type 1 motifs ADAMTS1	KIAA1346 protein	Unknown (protein for MGC:32979)	a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 15 preproprotein	metalloprotease disintegrin 15 with thrombospondin domains		DKFZP586G1122 protein	AF304052_1 hematopoietic zinc finger protein	DKFZP586G1122 protein	hypothetical protein DKFZp586G1122.1	hypothetical protein	unnamed protein product	hypothetical protein FLJ22419	unnamed protein product	AAH07212 hypothetical protein FLJ22419	unnamed protein product	hypothetical protein FL125270	umamed protein product	similar to zinc finger protein 385; hematopoietic zinc finger	himofletical amtein II 105070
NP_008919.2	AAF23772.1	BAA95502.1	AAD48080.1	ОЭПНІВ	AAF15317.1	BAA92584.1	AAH36515.1	NP_620686.1	CAC86014.1	XP_028643.4	NP_056296.1	AAL08625.1	AAH29752.1	T17248	CAB55938.1	BAB14910.1	NP 078973.1	BAB15350.1	AAH07212.1	BAC04870.1	NP 689733.1	BAB71629.1	XP_087103.1	A A H29477 1
				· ;;					ئارىيى	U:(C-IR) 2.01						÷		÷	-	٠		. <i>.</i>		
							:			Mm.1409 9				.:			.:	•			·		•	
										NM_013866 NP_038894.1	· .	\;;								·				

<u>.</u>			AAB59356.1	cytochrome		
			100000m	Syncation of the second of the	766	0
33.			P33260	CPCI_HUMAN Cytochrome P450 2C18 (CYPIIC18) (P450-6B/29C)	764	0
			A61269	cytochrome P450 2C18	764	C
		:	AAA02630.1	cytochrome P-4502C18	764	
			AAB23864.2	cytochrome P-450	726	
	:	:	NP_000762.2	cytochrome P450, subfamily IIC, polypeptide 9: cytochrome P450, subfamily IIC,	726	
	: ;			(mephenytoin 4-hydroxylase), polypeptide 10; mephenytoin 4-hydroxylase;	000/	<del>5</del> .
:				microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	•	
	. 1		P11712	CPC9_HUMAN Cytochrome P450 2C9 (CYPIIC9) (P450 PB-1) (P450 MP-4) (S-mephenytoin 4-hydroxylase) (P-450MP)	736	0
			B38462	S-mephenytoin 4-hydroxylase (EC 1.14.14) cytochrome P450 2C9	736	6
		h.	1313295A	cytochrome P450	736	0
			BAA00123.1	cytochrome P-450	. 736	0
			P11713	CPCA_HUMAN Cytochrome P450 2C10 (CYPIIC10) (P450 MP-8) (S-mephenytoin 4-hydroxylase) (P-450MP)	729	0 .
			D28951	cytochrome P450 2C10	729	0
	\	.	AAA52157.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	729	0
			AAA52158.1	cytochrome P-450 S-mephenytoin 4-hydroxylase	729	0
			1506290A	cytochrome P450	728	0
	1		NP_000760.1	cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 19; mephenytoin 4'-hydroxylase; microsomal monooxygenase; xenobiotic monooxygenase; flavoprotein-linked monooxygenase	726	0
		:	P33261	CPCJ_HUMAN Cytochrome P450 2C19 (CYPIIC19) (P450-11A) (Mephenytoin 4-hydroxylase) (CYPIIC17) (P450-254C)	726	0
			AAB59426.1	cytochrome	726	0
	:		F38462	S-mephenytoin 4'-hydroxylase (EC 1.14.14) cytochrome P450 2C19	722	C
	; .	U.(C-R)	CAA11218.1	36 kDa phosphothyrosine protein	231	2e-60
NM_010689 NP_034819.1	Mm.1028 0	U.(C.D) 2.17				
					-	

			AAC39636.1.	LAT	231	28-60
,		:	AAH11563.1	AAH11563 Similar to linker for activation of T cells	231	26-60
	:		NP 055202.1	linker for activation of T cells	215	1e-55
			043561	LAT_HUMAN Linker for activation of T cells (36 kDa phospho-tyrosine adaptor protein) (pp36) (p36-38)	215	1e-55
		•	AAC39637.1	LAT	215	10.55
NM_017370 NP_059066.1	Mm.2673 0	U:(C-D) 6.81	CAA25926.1	haptoglobin	. 599	e-171
			P00737	HPT1 HUMAN Haptoglobin-1 precursor	408	171
			HPHU1	haptoglobin precursor, allele 1 [validated]	. 598	e-171
		·	AAA52684.1	preprohaptoglobin	598	
	·	·	CAA25267.1	haptoglobin alpha 1S	598	239
			AAC27432.1	haptoglobin	597	e-170
			NP 066275.2	haptoglobin-related protein; Haptoglobin-related locus	569	e-162
	,		P00739	HPTR_HUMAN Haptoglobin-related protein precursor	569	e-162
:	• ;		HPHUR .	haptoglobin-related protein precursor	569	e-162
			AAA88079.1	haptoglobin-related protein	569	e-162
	·		AAA88081.1	haptoglobin-related protein	569	e-162
11.			CAA25927.1	haptoglobin	568	e-162
		·	AAC27433.1	haptoglobin-related protein precursor	565	e-161
	:	:	CAA61501.1	haptoglobin-related protein	565	e-161
. 1		::	AAA52687.1	haptoglobin precursor	559	e-159
		:	NP_005134.1	haptoglobin	559	e-159
	, ·		P00738	HPT2_HUMAN Haptoglobin-2 precursor	559	e-159
			HPHU2	haptoglobin precursor, allele 2	559	e-159
			CAA25137.1	haptoglobin precursor	559	e-159
		2.00	AAA88078.1	haptoglobin	559	e-159
			AAA88080.1	haptoglobin	559	e-150

	· :		AAA52685.1	preprohaptoglobin	559	e-159
		•	1006264A	haptoglobin Hp2	508	e-144
NIM_007424		U:(C-D) 4.11 U:(R-D)		aggrecan 1 isoform 2 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identifies by monoclonal antibody A0122);		
NP_031450.1	Mm.2759	3.08	NP_037359.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1795	0 .
. :			> ::::	aggrecan 1 isoform 1 precursor; Aggrecan-1 (chondroitin sulfate proteoglycan-1, large aggregating proteoglycan, antigen identifies by monoclonal antibody A0122):	•	
			NP_001126.1	chondroitin sulfate proteoglycan 1, large aggregating proteoglycan	1794	0
V (VX)		:	AAA62824.1	large aggregating cartilage proteoglycan core protein	1794	0
	: .		A39086	aggrecan precursor, cartilage long splice form	1792	0
			AAH36445.1	Similar to aggrecan 1 (chondroitin sulfate proteoglycan 1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122)	1253	0
			CAA35463.1	cartilage specific proteoglycan (600 AA)	823	0
			AAA35726.1	proteoglycan core protein	573	e-162
		•	AAH10571.1	chondroitin sulfate proteoglycan BEHAB/brevican	969	e-101
			AAG23134.1	AF228710_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	e-101
			AAG23135.1	AF229053_1 chondroitin sulfate proteoglycan BEHAB/brevican	369	. e-101
NM_009008	Mm 1072	U.(C-D)		ras-related C3 botulinum toxin substrate 2; Ras-related C3 botulinum toxin substrate 3 (tho family, small GTP-binding protein Rac2); tho family, small GTP binding protein		
14E 033034.1		7.03	INF 002803.1	Kac.	330	e-108
,			P15153	RAC2_HUMAN Ras-related C3 botulinum toxin substrate 2 (p21-Rac2) (Small G protein) (GX)	390	e-108
			B34386	GTP-binding protein rac2	390	e-108
	:1	· :	1DS6	A Chain A, Crystal Structure Of A Rac-Rhogdi Complex	390	e-108
	:	·	AAA36538.1	ras-related C3 botulinum toxin substrate	390	e-108
	:		AAB22207.1	rac1 p21=small GTP-binding protein [human, HL60, Peptide, 192 aa]	390	e-108
			CAB45265.1	dJ151B14.2 (ras-related C3 botulinum toxin substrate 2 (rho family, mall GTP binding protein Rac2))	. 390	e-108
			AAH01485.1	AAH01485 ras-related C3 botulimum toxin substrate 2 (rho family, small GTP binding protein Rac2)	390	e-108

			AAM21112.1	AF498965 1 small GTP binding protein RAC2	200	001
: .		·	NP_008839.2	ras-related C3 botulinum toxin substrate 1 isoform Rac1; rho family, small GTP binding protein Rac1	795	6-101
			P15154	RAC1_HUMAN Ras-related C3 botulimum toxin substrate 1 (p21-Rac1) (Ras-like protein TC25)	367	101
-	;		TVHUC1	GTP-binding protein rac1	367	-101
·			114D	D Chain D, Crystal Structure Analysis Of Rac1-Gdp Complexed With Arfaptin (P21)	367	e-101
			114L	D Chain D, Crystal Structure Analysis Of Rac1-Gdp In Complex With Arfaptin (P41)	. 367	e-101
			AAA36537.1	ras-related C3 botulinum toxin substrate	367	e-101
			AAB22206.1	rac1 p21=small GTP-binding protein [human, HL60, Peptide, 192 aa]	367	e-101
			CAB53579.5	Rac1 protein	. 367	e-101
			A:AM21111.1	AF498964_1 small GTP binding protein RAC1	367	e-101
	*		AAH04247.1	AAH04247 ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	367	-101
			AAA35941.1	small G protein	366	e-101
	:	• •	AAA36544.1	ras-like protein	366	e-101
			114T	D Chain D; Crystal Structure Analysis Of Rac1-Gmppnp In Complex With Arfaptin	365	e-100
	:		1e+96	A Chain A, Structure Of The RacP67PHOX COMPLEX	363	e-100
		• • •	1HH4	A Chain A, Rac1-Rhogdi Complex Involved In Nadph Oxidase Activation	362	e-100
			1HH4'	B Chain B, Rac1-Rhogdi Complex Involved In Nadph Oxidase Activation	362	e-100
	· }	•	NP_005043.1	ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3); rho family, small GTP binding protein Rac3	358	1e-98
			014658	RAC3_HUMAN Ras-related C3 botulinum toxin substrate 3 (p21-Rac3)	358	- 1e-98
	.		AAC51667.1	Rac3	358	1e-98
			AAH15197.1	AAH15197 ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)	358	1e-98
		*:-	AAH09605.1	AAH09605 ras-related C3 botulinum toxin substrate 3 (tho family, small GTP binding protein Rac3)	358	16-98
			AAM21113.1	AF498966 1 small GTP binding protein RAC3	358	1e-98

		:				,
			NP_061485.1	ras-related C3 botulinum toxin substrate 1 isoform Rac1b; rho family, small GTP binding protein Rac1	356	5e-98
	· .		CAA10732.1	small GTPase rac1b	356	56-98
			AAD30547.1	AF136373_1 ras-related C3 botulinum toxin substrate isoform	356	5e-98
· .			CAA10733.6	Racib protein	356	5e-98
AK013740	•					
BAB28979.1	U:(C Mm.27579 2.82	U:(C-D) 2.82	NP_068747.1	hypothetical protein FLJ22649 similar to signal peptidase SPC22/23	298	. 1e-80
		٠	BAB15437.1	unnamed protein product	298	16-80
•	:.		Q9H0S7	SP22_HUMAN Microsomal signal peptidase 23 kDa subunit (SPase 22 kDa subunit)	295	96-80
. 1	`.'	:	CAB66595.1	hypothetical protein	. 295	
X00496		U:(C-D) 2.81	NP_004346.1	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated); CD74 antigen (invariant polypeptide of major histocompatibility	226	242 65-94
CAMES 191.1	WIII. 7 043		CA A25100 1	class II antigen-associated)		•
			CAA23192.1	puranye p.5.3	226	4e-59
			AAA36033.1	cell surface glycoprotein	226	4e-59
· · · · · · · · · · · · · · · · · · ·	: ·.		AAH18726.1	AAH18726 CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	226	4e-59
,			HLHUG	class II histocompatibility antigen-associated gamma chain	226	46-59
			CAA25193.1	putative p33	226	4e-59
·	: :		AAA36304.1	class II antigen gamma chain	226	4e-59
			CAA27047.1	gamma chain	225	9e-59
1.			P04233	HG2A_HUMAN HLA class II histocompatibility antigen, gamma chain (HLA-DR antigens associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD74 antigen)	207	1e-53
	:	Ū:(C-Ď)	AAH36390.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	1078	0
NM_015737 NP_056552.1	Mm.5699	U:(IR-D)		4 (GalinAc-14)		

		NP_003765.1	polypeptide N-acetylgalactosaminyltransferase 4; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4; GalNAc transferase 4; UDP-GalNAc; polypeptide N-acetylgalactosaminyltransferase 4; N-acetylgalactosaminyltransferase 4	1073	0
 ÷		CAA69875.1	UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase	1073	0
	• -	CAC80100.2	UDP-GalNAc-transferase 12	624	e-178
		NP_078918.2	hypothetical protein FLJ21212; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12(GalNAc-T12)	622	e-178
· •		BAC07181.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	622	e-178
	:	NP_004473.1	polypeptide N-acetylgalactosaminyltransferase 3; protein-UDP acetylgalactosaminyltransferase	462	e-130
:		CAA63371.1	UDP-GallNAc:polypeptide N-acetylgalactosaminyltransferase (GallNAc-T3)	462	e-130
i ." : .	÷	AAH35822.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6)	461	e-129
		BAC11118.1	umamed protein product	461	e-129
		NP_009141.1	polypeptide N-acetylgalactosaminyltransferase 6; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6; UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 6; protein-UDP acetylgalactosaminyltransferase 6; GalNAc transferase 6	459	e-129
		CAA69876.1	UDP-GaINAc:polypeptide N-acetylgalactosaminyltransferase	459	e-129
		BAB67811:1	KIAA1918 protein	417	· e-116
		NP_065207.2	polypeptide N-acetylgalactosaminyltransferase 1; UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1; GaINAc-T1; GaINAc transferase 1; protein-UDP acetylgalactosaminyltransferase 1; UDP-GaINAc:polypeptide N-acetylgalactosaminyltransferase 1	416	e-116
		Q10472	PAGT_HUMAN Polypeptide N-acetylgalactosaminyltransferase (Protein-UDP acetylgalactosaminyltransferase) (UDP-GalNAc:polypeptide, N-acetylgalactosaminyltransferase) (GalNAc-T1)	416	.e-116
		JC4223	polypeptide N-acetylgalactosaminyltransferase (EC 2.4.1.41)	416	e-116
		CAA59380.1	UDP-GalNAc:polypeptide N-acetylgalactosaminyl transferase	416	e-116

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NM_018866 Mm.1011 NP_061354.1 6		U:(C-D) 2.65			·	
	• •					
NM_008458						
:	,	U:(C-D)	•			
NP 032484.1	Min.14191 2.59	2.59	CAA48671.1	alpha1-antichymotrypsin	494	e-139
•		•	XP_028322.1	similar to Alpha-1-antichymotrypsin precursor (ACT)	490	e-138
:		: .	P01011	AACT_HUMAN Alpha-1-antichymotrypsin precursor (ACT)	490	e-138
	•.	· · ·	AAH03559.1	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitypsin), member 3	490	e-138
			AAH10530.1	Unknown (protein for MGC:18102)	490	e-138
			AAH34554.1	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3	489	e-138
	· .	;	AAD08810.1	alpha-1-antichymotrypsin precursor	478	· e-134
:	1		TTHUC '	alpha-1-antichymotrypsin precursor	476	e-134
: .	. "	· :_	AAA51560.1.	alpha-1-antichymotrypsin precursor	. 470	e-132
,	· .	· ;	: :	A Chain A, Alpha1-Antichymotrypsin Serpin In The Delta Conformation (Partial		:
			10MN	Loop Insertion)	460	· e-129
:	. :	;	1313184C	chymotrypsin inhibitor	441	· e-123
		. :	NP-001076.1	alpha-1-antichymotrypsin, precursor; alpha-1-antichymotrypsin; antichymotrypsin	439	e-123
		. 1	AAA51543.1	alpha-1-antichymotrypsin	439	e-123
	:		2ACH	A Chain A, Alpha 1 Antichymotrypsin	434	e-121
NM_010382 NP_034512.1	Mm.2256 4	U:(C-D) 2.59	AAH07920.1	AAH07920 Unknown (protein for MGC:14111)	390	e-108
			AAL40069.1	L76133_1 lymphocyte antigen	390	e-108
			AAH08403.1.	AAH08403 Similar to major histocompatibility complex, class II, DR beta 5	387	e-107
			CAC08827.1	MHC class II antigen	386	e-107
	1. 6.1		I54448 ····	MHC class II histocompatibility antigen DR beta 1 chain precursor	386	e-107
			AAA59713.1	precursor	386	e-107

			CAC08823.1	MHC class II antigen	386	e-107
		:	P20039	HB21_HUMAN HLA class II histocompatibility antigen, DR-5 beta chain precursor	385	e-107
			A25324 ·	class II histocompatibility antigen HLA-DR-5 beta chain precursor	385	e-107
: 1	; ;;		AAA36274.1	MHC HLA DR5 cell surface glycoprotein beta chain precursor	385	e-107
			CAC08826.2	MHC class II antigen	385	· e-107
			P13760	HB2H HUMAN HLA class II histocompatibility antigen, DR-4 beta chain precursor (DRB1*0401)	385	e-107
	:		A29310.	MHC class II histocompatibility antigen HLA-DR beta 1 chain DR4 precursor	385	e-107
			CAC19360.1	d1863G3.2 (major histocompatibility complex, class II, DR beta 1)	385	e-107
		·	CAB75359.1	human leucocyte antigen DRB1	385	e-107
	·	;	P01912	HB2B_HUMAN HLA class II histocompatibility antigen, DR-1 beta chain precursor (Clone P2-beta-3)	385	.e-107
	;			pir  HLHU3D MHC class II histocompatibility antigen HLA-DR beta 1 chain DR17 precursor	385	e-107
	;	÷	CAA25295.1	precursor	385	e-107
			CAB06490.1	d193N13.3 (major histocompatibility complex, class II, DR beta 1 (clone P2-beta-3))	385	e-107
:	•					
AK012581						
XP_126675.1	D):D	U.(C-D)				
	, 10017 min	2.33	AM 006067 1	nypouneucai protein 55143	240	2e-63
				aypomencai protein ivigici 10986	240	2e-63
			AAH04400.1	Unknown (protein for MGC:10986)	. 240	2e-63
	·	•	BAC03855.1	unnamed protein product	240	2e-63
	!	U:(C-D)	NP_690591.1	membrane-spanning 4-domains, subfamily A, member 6A isoform 1; CD20-like	233	5e-61
NM_027209 NP_081485.1	Mm.2948 7			transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso	•	<del></del>
			AAG41780,1	AF212240_1 CDA01	233	5e-61
			AAK37417.1	AF237908 1 MS4A6A protein	. 233	.5e-61
						-

			AAK37994.1	AF286866 1 MS4A6A-polymorph	233	58-61
				membrane-spanning 4-domains, subfamily A, member 6A	232	8e-61
			AAL56222.1	AF350502_1 four-span transmembrane protein 3.1	229	5e-60
			AAG44626.Ï	AF253977_1 HAIRB-iso	222	1e-57
			NP_071744.2	membrane-spanning 4-domains, subfamily A, member 6A isoform 2; CD20-like precusor: membrane-spanning 4-domains, subfamily A member 6; four-span	208	1e-53
				transmembrane protein 3.2; MS4A6A-polymorph; four-span transmembrane protein 3.1; HAIRB-iso	٠	•
			AAL07357.1	AF354930_1 MS4A6A	208	1e-53
	; ; ; ;		AAG27920.1	AF142409_1 CD20-like precusor	207	2e-53
			AAL56223.1	AF350503_1 four-span transmembrane protein 3.2	207	. 4e-53
NM_011116	11 E102	U:(C.D)	AAH36327.1	Similar to phospholipase D3	890	246
110-720-101	1.		AAH00553.1	AAH00553 similar to vaccinia virus HindIII K4L ORF	818	0
			NP_036400.1	similar to vaccinia virus HindIII K4L ORF	816	0
			AAB16799.1	HU-K4	816	0
	• •	: .	NP_620145.1	hypothetical protein BC015003	385	· e-106
			AAH15003.1	AAH15003 Unknown (protein for MGC:23565)	385	e-106
			NP_689879.1	hypothetical protein FLJ40773	275	2e-73
			BAC05230.1	unnamed protein product	275	2e-73
			BAC03722.1	unnamed protein product	223	9e-58
NM_013487 NP_038515.1	Mm.4527	U.(C-D) 2.39	NP_000723.1	CD3D antigen, delta polypeptide (TiT3 complex)	228	5e-60
			P04234	CD3D_HUMAN T-cell surface glycoprotein CD3 delta chain precursor (T-cell receptor T3 delta chain)	. 728	5e-60
: :	: :	:	RWHUD1	T-cell surface glycoprotein CD3 delta chain precursor	228	. 5e-60
	, ,		CAA25683.1	20K T3 glycoprotein precursor	228	5e-60
			AAA51792.1	T3 antigen delta-chain	228	. 5e-60
<u>.</u>			CAA27573.1	T3 delta protein	228	2e-60

·	1150							1150 1150 1141 1950 1950 1949 892 892 892	1150     0       1150     0       1141     0       1950     0       1950     0       892     0       892     0       892     0       892     0       892     0       892     0       892     0       892     0       892     0       893     2e-75       283     2e-75       283     2e-75	1150     0       1150     0       1141     0       1950     0       1949     0       892     0       892     0       283     2e-75       283     2e-75       283     2e-75       283     2e-75	1150     0       1150     0       1141     0       1950     0       1949     0       892     0       892     0       283     2e-75       283     8e-62	1150     0       1150     0       1141     0       1950     0       1949     0       892     0       892     0       283     2e-75       283     2e-75       283     2e-75       283     2e-75       283     8e-62       761     0	1150 0 1150 0 1141 0 1950 0 1950 0 892 0 892 0 892 0 892 0 892 0 892 0 893 2e-75 283 2e-75 283 2e-75 283 2e-75 761 0	1150     0       1150     0       1141     0       1950     0       1949     0       892     0       892     0       283     2e-75       283     2e-75       283     2e-75       283     8e-62       761     0       751     0       751     0	1150 0 1150 0 1141 0 1141 0 1950 0 1949 0 892 0 892 0 892 0 892 0 892 0 892 0 783 2e-75 283 2e-75 283 2e-75 283 2e-75 761 0 751 0	1150 0 1150 0 1141 0 1141 0 1950 0 1949 0 892 0 892 0 892 0 892 0 892 0 783 2e-75 283 2e-75 283 2e-75 761 0 751 0 751 0	1150 00 1150 00 11141 00 1141 00 11950 00 1950 00 892 00 892 00 892 00 892 00 783 2e-75 283 2e-75 283 2e-75 283 2e-75 751 00 751 00 751 00 751 00	1150 0 1150 0 1141 0 1141 0 1950 0 1949 0 892 0 892 0 892 0 892 0 783 2e-75 283 2e-75 283 2e-75 283 2e-75 751 0 751 0 751 0 751 0 751 0 751 0	1150 1150 1141 1950 1950 1949 892 892 892 26-7 283 26-7 283 26-7 751 751 751 751 751 751 751 751 751
						1)	1)	t 1)	1)	1)	1)	placement protein	of 1)	in 1)	placement protein	placement protein	placement protein	1) placement protein	1) placement protein
			-like 2)	-like 2)	-like 2)	KIAA0710 protein  KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 1)	-like 2) (CDP) (Cut-like 1) ptide, 1505 aa]	KIAA0710 protein  KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 1)  CCAAT displacement protein, CDP [human, Peptide, 1505 aa]  cut-like 1, CCAAT displacement protein; cut like 1, CCAAT displacement protein  (Drosophila)	-like 2) (CDP) (Cut-like 1) ptide, 1505 aa] e 1, CCAAT displace	t-like 2)  (CDP) (Cut-like 1)  ptide, 1505 aa]  e 1, CCAAT displace	-like 2) (CDP) (Cut-like 1) ptide, 1505 aa] te 1, CCAAT displace	t-like 2)  (CDP) (Cut-like 1)  ptide, 1505 aa]  e 1, CCAAT displace	r-like 2) (CDP) (Cut-like 1) ptide, 1505 aa] e 1, CCAAT displace phila)	-like 2)  (CDP) (Cut-like 1)  ptide, 1505 aa]  e 1, CCAAT displace  phila)  phila)	c 1, CCAAT displace	-like 2)  (CDP) (Cut-like 1)  ptide, 1505 aa]  e 1, CCAAT displace  phila)  1999full	c 1, CCAAT displace	KIAA0710 protein KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 1)  CCAAT displacement protein; cut like 1, CCAAT displacement protein; cut-like 1, CCAAT displacement protein; cut-like 1, CCAAT displacement protein; cut-like 1, CCAAT displacement protein for MGC:17861)  ARZ71236_1 transcription factor CUX2  hypothetical protein  AAHI5234 Unknown (protein for MGC:17861)  ARH15234 Unknown  bA351K23.5 (novel protein)  diacylglycerol 0-acyltransferase 2 like 1; diacylglycerol acyltransferase 2-like 2-like	r-like 2)  (CDP) (Cut-like 1)  ptide, 1505 aa]  e 1, CCAAT displace phila)  phila)  glycerol acyltransfers  ke protein
	•	١.	ein Cux-2 (Cut-lik	ein Cux-2 (Cut-lik IX-2	ix-2 (Cut-like 2)	ein Cux-2 (Cut-lik IX-2 c-2 (Cut-like 2)	tein Cux-2 (Cut-lik IX-2 c-2 (Cut-like 2) cement protein (CI	ein Cux-2 (Cut-lik IX-2  c-2 (Cut-like 2)  cement protein (CI DP [human, Peptid protein; cut like 1,	tein Cux-2 (Cut-lik UX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1,	ux-2  ix-2  ix-2  ix-2  ix-1 (Cut-like 2)  cement protein (CI  protein; cut like 1,  protein (Drosophil	ein Cux-2 (Cut-lik UX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophi) CUX2	ux-2  c-2 (Cut-like 2)  c-2 (Cut-like 2)  cement protein (CI  protein; cut like 1,  protein (Drosophil  CUX2	ein Cux-2 (Cut-lik IIX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophi) CUX2 homolog 2; GS199	tein Cux-2 (Cut-lik UX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophil CUX2 homolog 2; GS199 ar MGC:17861)	ein Cux-2 (Cut-lik IK-2  E-2 (Cut-like 2)  cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophi) CUX2  r MGC:17861)  transferase 2	tein Cux-2 (Cut-lik uX-2 c-2 (Cut-like 2) cement protein (CL DP [human, Peptid protein; cut like 1, protein (Drosophil CUX2 cUX2 homolog 2; GS199 or MGC:17861) transferase 2	ein Cux-2 (Cut-lik IX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophi CUX2 r MGC:17861) transferase 2	ein Cux-2 (Cut-lik uX-2 c-2 (Cut-like 2) cement protein (CI DP [human, Peptid protein; cut like 1, protein (Drosophil CUX2 n MGC:17861) transferase 2 transferase 2 like 1; diacylgly	ein Cux-2 (Cut-lik LIX-2 c-2 (Cut-like 2) cement protein (CL DP [human, Peptid protein; cut like 1, protein (Drosophi) CUX2 r MGC:17861) transferase 2 2 like 1; diacylglye transferase 2-like p
e product		e product	e product N Homeobox prote	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cul The human homolog of mouse Cux-2 similar to Homeobox protein Cux-2 (Cut-like 2)	e product  N Homeobox prote  olog of mouse Cur  cobox protein Cux-  N CCAAT displace	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP) (Cut-like 2)  CCAAT displacement protein, CDP [human, Peptide, 1505 aa]	e product  N Homeobox prote  sobox protein Cux- N CCAAT displace cement protein, CD	e product  N Homeobox prote  1010g of mouse Cur- cobox protein Cux- N CCAAT displace sement protein, CD  AT displacement p  iced	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like; The human homolog of mouse Cux-2  similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP CCAAT displacement protein; cut like 1, C  Drosophila)  alternatively spliced  cut-like 1, CCAAT displacement protein; cut like 1, C  drosophila)	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cu  The human homolog of mouse Cux-2 similar to Homeobox protein Cux-2 (Cu  CUT1_HUMAN CCAAT displacement CCAAT displacement protein, CDP [hu cut-like 1, CCAAT displacement proteir (Drosophila) alternatively spliced cut-like 1, CCAAT displacement proteir AF271236_1 transcription factor CUX2	e product  N Homeobox prote sobox protein Cux- cement protein, CD  AT displacement p  AT displacement p  anscription factor of	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  Similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP) (CCAAT displacement protein; cut like 1, CCA(Drosophila)  alternatively spliced  cut-like 1, CCAAT displacement protein; cut like 1, CCA(Drosophila)  AF271236_1 transcription factor CUX2  hypothetical protein  diacylglycerol O-acyltransferase homolog 2; GS1999full	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut The human homolog of mouse Cux-2 similar to Homeobox protein Cux-2 (Cut-like 2) CUT1_HUMAN CCAAT displacement protein CCAAT displacement protein; cut lik (Drosophila) alternatively spliced cut-like 1, CCAAT displacement protein (Droso AF271236_I transcription factor CUX2 hypothetical protein diacylglycerol O-acyltransferase homolog 2; GS AAH15234 Unknown (protein for MGC:17861)	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (C The human homolog of mouse Cux-2 (Cut-like cut-like 1, CCAAT displacement protein Cux-displacement protein Cut-like 1, CCAAT displacement protein; cut (Drosophila)  alternatively spliced cut-like 1, CCAAT displacement protein (Drosophila)  alternatively spliced cut-like 1, CCAAT displacement protein (Drosophila)  AF271236_1 transcription factor CUX2  hypothetical protein  diacylglycerol O-acyltransferase homolog 2; (AAH15234 Unknown (protein for MGC:1786  AF384161_1 diacylglycerol acyltransferase 2	e product  N Homeobox prote sobox protein Cux- cement protein, CD  AT displacement p  AT displacement p  anscription factor of tein  Covan (protein for acylgransferase h  known (protein for acylglycerol acyltr	e product lollog of mouse Cur- cobox protein Cux- N CCAAT displace cement protein, CD AT displacement priced AT displacement protein anscription factor ( anscription factor ( beaufitansferase h known (protein for acylglycerol acyltr own own	e product  N Homeobox prote sobox protein Cur- cement protein, CD  AT displacement p  AT displacement p  anscription factor of tein  Cover protein for acylgransferase h  known (protein for acylgransferase h  cover protein)  D-acyltransferase 2  Over protein)	KIAA0710 gene product  CUT2_HUMAN Homeobox protein Cux-2 (Cut-like 2)  The human homolog of mouse Cux-2  Similar to Homeobox protein Cux-2 (Cut-like 2)  CUT1_HUMAN CCAAT displacement protein (CDP) (C  CCAAT displacement protein, CDP [human, Peptide, 150  CUT1_HUMAN CCAAT displacement protein; cut like 1, CCA  (Drosophila)  alternatively spliced  cut-like 1, CCAAT displacement protein (Drosophila)  AF271236_I transcription factor CUX2  hypothetical protein  diacylglycerol O-acyltransferase homolog 2; GS1999full  AAH15234 Unknown (protein for MGC:17861)  AF384161_I diacylglycerol acyltransferase 2  product is unknown  bA351K23.5 (novel protein)  diacylglycerol O-acyltransferase 2 like 1; diacylglycerol acyltransferase 2-like protein
KIAA0710 gene product	A A A C C C C C C C C C C C C C C C C C	KIAA0710 gene	KIAA0710 gene product	KIAA0710 gene r CUT2_HUMAN The human homo	KIAA0710 gene I CUTZ HUMAN The human homol	KIAA0710 gene provide to the human homo similar to Homeol CUT1_HUMAN	KIAA0710 gene I CUT2_HUMAN The human homol similar to Homeol CUT1_HUMAN CCAAT displace	KIAA0710 gene I CUTZ_HUMAN I Similar to Homeol CUT1_HUMAN CCAAT displace cut-like 1, CCAA (Drosophila)	KIAA0710 gene pro CUT2_HUMAN Ho Similar to Homeoboo CUT1_HUMAN CC CCAAT displaceme cut-like 1, CCAAT (Drosophila) alternatively spliced	KIAA0710 gene I CUTZ HUMAN The human homol similar to Homeol CUT1 HUMAN CCAAT displace cut-like 1, CCAA alternatively splic cut-like 1, CCAA	KIAA0710 gene I CUT2_HUMAN Similar to Homeol CUT1_HUMAN CCAAT displacer cut-like 1, CCAA (Drosophila) alternatively splic cut-like 1, CCAA Cut-like 1, CCAA AFZ71236_1 tran	KIAA0710 gene pro CUTZ_HUMAN Ho The human homolog similar to Homeoboy CUT1_HUMAN CC CCAAT displaceme cut-like 1, CCAAT of Drosophila) alternatively spliced out-like 1, CCAAT of AFZ71236_1 transcr	KIAA0710 gene I CUT2_HUMAN I The human homol similar to Homeol CUT1_HUMAN CCAAT displace cut-like 1, CCAA displace alternatively splic cut-like 1, CCAA dernatively splic cut-like 1, CCAA dernatively splic diacyletical prote	KIAA0710 gene I CUT2_HUMAN I Similar to Homeol CUT1_HUMAN OCCAAT displace CUT-like 1, CCAA GDrosphila) alternatively splic cut-like 1, CCAA AF271236_I tran hypothetical prote diacylglycerol O- AAH15234 Unkn	KIAA0710 gene processival and	KIAA0710 gene pro CUT2_HUMAN Ho Similar to Homeobo CUT1_HUMAN CC CCAAT displaceme cut-like 1, CCAAT alternatively spliced out-like 1, CCAAT AF271236_1 transc hypothetical protein diacylglycerol O-ac AAH15234 Unkmov AF384161_1 diacyl product is unknown	KIAA0710 gene product  CUTZ_HUMAN Homeobox The human homolog of mous similar to Homeobox protein CUT1_HUMAN CCAAT dis CUT1_HUMAN CCAAT dis CUT1_HUMAN CCAAT dis cut-like 1, CCAAT displacer (Drosophila) alternatively spliced cut-like 1, CCAAT displacer AF271236_1 transcription fa hypothetical protein diacylglycerol O-acyltransfer AAH15234 Unknown (prote AF384161_1 diacylglycerol product is unknown bA351K23.5 (novel protein)	KIAA0710 gene I CUT2_HUMAN I Similar to Homeol CUT1_HUMAN OCCAAT displace CUT-like 1, CCAA of Opposible 1, CCAA of	KIAA0710 gene processor and pr
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	251	219	215	206	206		1081	956	926	926	.954	954		. 286	. 286	286	286	. 284	284	284	258	200	199		388
	similar to bA351K23.5 (novel protein)	similar to bA351K23.5 (novel protein)	similar to bA351K23.5 (novel protein)	hypothetical protein FLJ22644	unnamed protein product		ezzin-binding protein PACB-1	bypothetical protein	dJ97P20.1 (novel gene)	ezzin-binding partner PACE-1	ezrin-binding partner PACE-1	Similar to hypothetical protein LOC57147		similar to P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	SEPL_HUMAN P-selectin glycoprotein ligand 1 precursor (PSGL-1) (Selectin P ligand) (CD162 antigen)	P-selectin glycoprotein ligand PSGL-1 precursor, long splice form	P-selectin glycoprotein ligand	selectin P ligand	ligand for P-selectin	selectin P ligand	unnamed protein product	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F; similar to Phorbolin 3 (APOBEC1-like)	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F		KIAA1543 protein
	XP 088691.1	XP_088683.1	XP_093119.2	NP_079374.1	BAB15436.1		AAN41656.1	CAB55300.1	CAB52564.2	AAN23123.1	NP_065156.4	AAH14662.1		XP_006867.4	Q14242	A57468	AAA74577.1	NP_002997.1	AAC50061.1	AAH29782.1	BAC05283.1	NP_660341.2	AAH38808.1	· .	BAA96067.1
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	CAA64079.1	2207224A	P51160 · ·	AAA92886.1	NP_006195.2	AAA96392.1	NP_000274.1	P35913	A42828	AAB22690.1	CAA46932.1	AAH00249.1	CAA44569.1	B34611	NP_000431.1	P16499	AAB69155.1	CAA62215.1	NP_058649.2	BAB16371.1	BAB62712.1	1 COP 200 MK	INE DUOTOS.I
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A STATE OF THE PERSON OF THE P	ALAS_HUMAIN Homeobox protein aristaless-like 3 (Froune-fich transcription ractor ALX3)	homeobox protein	solute carrier family 7, member 10; asc-type amino acid transporter 1	AAA1_HUMAN Asc-type amino acid transporter 1 (Asc-1)	asc-type amino acid transporter 1	AF340165_1 amino acid transporter	ASC1 protein	similar to solute carrier family 7	LAT2_HUMAN Large neutral amino acids transporter small subunit 2 (L-type amino acid transporter 2) (hLAT2)	AF171669_1 glycoprotein-associated amino acid transporter LAT2	L-type amino acid transporter 2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	SLC7A8 protein	AF135828_1 L amino acid transporter-2; LAT-2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 5; Membrane protein B16; Solute carrier family 7, member 5; 4F2 light chain	LAT1_HUMAN Large neutral amino acids transporter small subunit 1 (L-type amino acid transporter 1) (4F2 light chain) (4F2 LC) (4F2LC) (CD98 light chain) (Integral membrane protein E16) (hLAT1)	LAT1 protein	CD98 light chain	L-type amino acid transporter subunit LAT1	L-type amino acid transporter 1	amino acid transporter B16	Similar to solute carrier family 7 (cationic amino acid transporter, y+ system), member 5
	095076	AAD01418.1	NP_062823.1	O9NS82	BAB03213.1	AAK93960.1	CAC81900.1	AAH35627.1	०९णमार्ड	AAF20381.1	BAB21519.1	NP_036376.1	CAB40137.1	AAF05695.1	NP_003477.2	Q01650	JG0165	BAA33851.1	AAD20464.1	BAA84648.1	AAC61479.1	AAH39692.1
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i.	:		BAA75746.1	4F2 light chain	434	e-121
			BAB70708.1	sodium-independent neutral amino acid transporter LAT1	434	e-121
. ,			NP_003974.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	431	e-120
			BAA13376.1	Similar to Schistosoma mansoni amino acid permease (L25068).	. 431	e-120
		;	AAH28216.1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 6	. 431	e-120
AK018130	: :					
· · · ·		U:(C-D)				,
BAB31085.1	Mm.5202 2.13	2.13	D59433	C. elegans protein Z37093 homolog [imported]	. 739	0
:		;	BAA13212.1	similar to C.elegans protein (Z37093)	739	0
			AAC03237.1	D1013901	. 739	0
			XP_037574.1	similar to PTPL1-associated RhoGAP 1	739	0
		1	AAN04658.1	minor histocompatibility antigen HA-1	739	252
			AAH35564.1	Similar to PTPL1-associated RhoGAP 1	739	0
			NP_004806.1	PTPL1-associated RhoGAP 1	278	2e-74
}; ;; ;;	. : !	·i	E59430	PTPL1-associated RhoGAP protein 1 [imported]	278	2e-74
	:	•	AAB81012.1	PTPL1-associated RhoGAP	278	2e-74
			NP 057657.1	Gem-interacting protein	. 265	2e-70
	· •		D59435	Gem-interacting protein [imported]	265	2e-70
			AAF61330.1	AF132541_1 Gem-interacting protein	265	2e-70
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BAB29271.1	Mm.30114	0:(ヘン) 2.12	AAL14103.1	AF391100_1 alsin	1569	, 0
			BAB13389.2	KIAA1563 protein	1569	0
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1			BAB69014.1	long form	1569	0
			NP_667340.1	hypothetical protein LOC259173	244	. Se-64
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AK014599	:					
BAB29454.1	Mm.66017	U:(C-D) 2.12	AAD43186.1	AC006029_1 Similar to Sperm Surface Protein PH-20;Similar to P38568 (PID:585674)	749	0
			NP 036401.1	hyaluronoglucosaminidase 4; hyaluronidase 4	749	0
	•		AAC98833.1	hyaluronidase 4	749	0
		· :	NP 694859.1	sperm adhesion molecule 1 isoform 2; sperm surface protein PH-20; hvaluronoslucosaminidase	385	106
		. \		HYAP HUMAN Hvaluronidase PH-20 mecursor (Sperm surface protein PH-20)	3	
	;	·	P38567	(Sperm adhesion molecule 1)	385	e-106
	:		CAA59086.1	sperm adhesion molecule gene SPAM1	385	e-106
			NP_003108.2	sperm adhesion molecule 1 isoform 1; sperm surface protein PH-20; hyaluronoglucosaminidase	385	e-106
,			AAH26163.1	sperm adhesion molecule 1 (PH-20 hyaluronidase, zona pellucida binding)	385	e-106
			AAC60607.2	PH-20	382	e-105
·	:		S40465	sperm protein PH-20	382	e-105
		.1	AAD24460.1	AF118821_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
			AAD53277.1	AF173154_1 hyaluronoglucosaminidase 1 isoform 2	337	9e-92
	; ; . ;		NP_009296.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	16-91
:	# <del> </del>		NP_149349.2	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	336	16-91
		·	NP_695013.1	hyaluronoglucosaminidase 1 isoform 1; hyaluronidase 1; tumor suppressor LUCA-1; plasma hyaluronidase; hyaluronoglucosaminidase	. 336	. 16-91
		;	AAD04190.1	hyaluronoglucosaminidase 1	336	1e-91
: .			AAD09137.2	putative tumor suppressor	336	16-91
<i>;</i>		::	AAH35695.1	hyaluronoglucosaminidase 1	. 336	1e-91
	1		JC5584	hyalurononglucosaminidase (EC 3.2.1.35) 1 precursor	333	7e-91
NM_008969	7000	U.(C-D)		rostaglandin-endoperoxide synthase 1, isoform 1 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin		
117 076273.1		77.71	INF 000955.2	synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	1043	

. 1		0	0	0	0	0	0		0	254	0	. 0	. 0	0	0		0	0	0	0
	:				,				,							•				•
		T043	1043	1043	1043	1043	1043	1043	1038	956	956	. 729	729	729	729	729	729	729	729	727
		_	1	-												,	70			
	PGH1_HUMAN Prostaglandin G/H synthase 1 precursor (Cyclooxygenase -1) (COX-1) (Prostaglandin-endoperoxide synthase 1)	(PGH synthase 1) (PGHS-1) (PHS 1)	prostaglandin-endoperoxide synthase (EC.1.14.99.1) 1 precursor	prostaglandin endoperoxide synthase	prostaglandin endoperoxide synthase; cyclooxygenase	prostaglandin G/H synthase; PGG/HS	AF440204_1 prostaglandin-endoperoxide synthase 1	Unknown (protein for MGC:34214)	prostaglandin-endoperoxide synthase-1	prostaglandin-endoperoxide synthase 1, isoform 2 precursor; prostaglandin G/H synthase and cyclooxygenase; PGH synthase 1; PG synthetase; prostaglandin synthetase; cyclooxygenase-1; prostaglandin H2 synthetase 1	prostaglandin G/H synthase; PGG/HS	prostaglandin-endoperoxide synthase 2 precursor; prostaglandin G/H synthase and cyclooxygenase; cyclooxygenase-2; endoperoxide synthase type I; prostaglandin synthase-2; PG synthetase	PGH2_HUMAN Prostaglandin G/H synthase 2 precursor (Cyclooxygenase -2) (COX-2)(Prostaglandin-endoperoxide synthase 2) (Prostaglandin H2 synthase 2) (PGH synthase 2) (PGHS-2) (PHS II)	cyclooxygenase-2	prostaglandin endoperoxide synthase-2	PTGS2 (prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase))	AAH13734 prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	prostaglandin-endoperoxide synthase (EC 1.14.99.1) 2 precursor	cyclooxygenase-2	endoperoxide synthase type $\Pi$
	:	P23219	JH0259	AAA03630.1	AAB21215.1	AAB22217.1	AAL33601.1	AAH29840.1	AAA36439.1	NP 542158.1	AAB22216.1	NP_000954.1	P35354	AAA57317.1.	BAA05698.1	CAB41240.1	AAH13734.1	A46150	AAA58433.1	AAA35803.1
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NM_010225 NP_034355.1	Mm.6260	U:(C-D) 2.11	NP_001443.1	forkhead box F2; forkhead (Drosophila)-like 6	521	e-147
			Q12947	FXF2_HUMAN Forkhead box protein F2 (Forkhead-related protein FKHL6) (Forkhead-related transcription factor 2) (FREAC-2) (Forkhead-related activator-2)	521	e-147
		-	T09474	forkhead protein FREAC-2	521	e-147
			AAG32226.1	forkhead protein FREAC-2	521	e-147
			AAD19875.1	forkhead transcription factor	521	e-147
		:	2208384B	transcription factor FREAC-2	508	e-143
. , .			NP_001442.1	forkhead box F1; forkhead (Drosophila)-like 5; Forkhead, drosophila, homolog-like 5; forkhead-related activator 1 IHomo	<u> </u>	3e-66
:				sapiens]		
			Q12946	FXF1_HUMAN Forkhead box protein F1 (Forkhead-related protein FKHLS) (Forkhead-related transcription factor 1) (FRBAC-1) (Forkhead-related activator-1)	251	3e-66
· .	,		AAC50399.1	FREAC-1	251	3e-66
•			AAC61576:1	forkhead transcription factor	251	3e-66
		: '	2208384A	transcription factor FREAC-1	251	3e-66
NM_028770 NP_083046.1	Mm.3338 5	U:(C-D) 2.1	XP_096612.2	similar to RIKEN cDNA 1200016G03	561	e-159
			CAB76832.1	cytokeratin	270	66-72
,	1		NP_004684.1	cytokeratin type II -	270	1e-71
·			CAA76730.1	cytokeratin type II	270	16-71
: · · · · · · · · · · · · · · · · · · ·	; ; ;		AAH24292.1	keratin 5 (epidermolysis bullosa simplex, Dowling-Meara/Kobner/Weber-Cockayne types)	. 261	. 5e-69
			AAA36145.1	keratin K.5	260	7e-69
			NP_000415.1	keratin 5; Keratin-5; 58 kda cytokeratin; keratin, type II cytoskeletal 5; cytokeratin 5	.260	7e-69
	:		P13647	K2C5_HUMAN Keratin, type II cytoskeletal 5 (Cytokeratin 5) (K5) (CK 5) (58 kDa cytokeratin)	260	7e-69
· .			A29904	keratin 5, type II, epidermal	260	7e-69
.			AAA36143.1	keratin type II	260	7e-69
			AAF97931.1	AF274874 1 keratin 5	260	7e-69

·:		NP_002264.1	keratin 8; Keratin-8	250	16.68
	:	CAA52882.1	Keratin 8	259	16-68
		AAB18966.1	human cytokeratin 8	259	16-68
		AAH00654.1	AAH00654 keratin 8	259	1e-68
		A34720	keratin 8, type II cytoskeletal	259	1e-68
:		P05787	K2C8 HUMAN Keratin, type II cytoskeletal 8 (Cytokeratin 8) (K8) (CK 8)	259	1e-68
		AAA35763,1	cytokeratin 8	259	1e-68
Mm.1444 13		U:(C-D) NP_003346.2 2.09	uncoupling protein 2	585	e-167
;		P55851	UCP2_HUMAN Mitochondrial uncoupling protein 2 (UCP 2) (UCPH)	. 585	e-167
		AAC51336.1	UCP2	585	
		AAC39690.1	uncoupling protein 2	585	256
•		AAD21151.1	uncoupling protein-2	. 585	e-167
		AAH11737.1	AAH11737 uncoupling protein 2 (mitochondrial, proton carrier)	585	e-167
		AAB53091.1	uncoupling protein homolog	583	e-166
		CAA11402.1	uncoupling protein 2	583	e-166
ا :		AAB48411.1	uncoupling protein-2	583	e-166
		NP_003347.1	uncoupling protein 3, isoform UCP3L	451	e-127
		P55916.	UCP3_HUMAN Mitochondrial uncoupling protein 3 (UCP 3)	451	e-127
		JC5522	uncoupling protein UCP3, mitochondrial	451	e-127
		AAC51367.1	UCP3	451	e-127
		AAC51369.1	uncoupling protein 3	451	e-127
	;	AAC51767.1	uncoupling protein-3	451	e-127
		AAG02284.1	AF050113_1 uncoupling protein-3	451	e-127
		AAC18822.1	uncoupling protein 3	445	e-125
:		AAC51785.1	uncoupling protein 3	. 432	· e-121
		NP_073714.1	uncoupling protein 3, isoform UCP3S	392	e-109
	•	AAC51356.1	UCP3S	302	P-100
					- / / /

		·	NP 068605.1	uncoupling protein 1; mitochondrial brown fat uncoupling protein	353	. 2e-97
			G01858	uncoupling protein 1, mitochondrial	353	2e-97
			AAA85271.1	uncoupling protein	353	2e-97
			P25874	UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (UCP 1) (Thermogenin)	350	2e-96
			CAA36214.1	uncoupling protein	250	2e-96
			AAH08392.1	AAH08392 Similar to uncoupling protein 3 (mitochondrial, proton carrier)	206	5e-53
NM_011933 NP_036063.1	Mm.3576 0	U.(C-D) 2.09	NP_065715.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
			CAB92744.1	c359F1.1 (novel protein (ortholog of mouse and rat peroxisomal 2,4-dienoyl-coA reductase (PDCR, DCR-AKL)))	466	e-131
		`. '	CAC05664.1	peroxisomal 2,4-dienoyl-CoA reductase	466	e-131
	:		AAK61231.1	AE006463_11 2-4-dienoyl-Coenzyme A reductase 2 peroxisomal like	466	e-131
		1	AAH10740.1	AAH10740 2,4-dienoyl CoA reductase 2, peroxisomal	797	e-131
			AAH11968.1	AAH11968 Similar to 2,4-dienoyl CoA reductase 2, peroxisomal	370	e-102
NM_019424 NP_062297.1	Mm.1948 06	U:(C-D) 2.08	AAL50684.1	AF450133_1 Hermansky-Pudlak syndrome	1065	0
			NP_000186.1	Hermansky-Pudlak syndrome protein; Hermansky-Pudlak syndrome gene; Hermansky-Pudlak syndrome	1064	0
•	:		Q92902	HPS1_HUMAN Hermansky-Pudlak syndrome 1 protein	1064	0
	·	•	AAB17869.1	Hermansky-Pudlak syndrome protein	1064	0
			AAB70662.1	Hermansky-Pudlak syndrome protein	. 998	0
			AAH00175.1	AAH00175 Hermansky-Pudlak syndrome	411	e-114
	;	 	AAC52074.1	alternative Hermansky-Pudlak syndrome associated protein	409	e-114
<i>:</i>						
NM_008433			•			
NP_032459.1	Mm.9911	U:(C-D) 2.06	NP_002241.1	intermediate conductance calcium-activated potassium channel protein 1; putative erythrocyte intermediate conductance calcium-activated potassium Gardos channel	209	e-173
			015554	KCN4_HUMAN Intermediate conductance calcium-activated potassium channel protein 4 (SK4) (KCa4) (IKCa1) (Putative Gardos channel)	209	e-173

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	•	٠	AAB82739.1	calcium-activated potassium channel	607	e-173
	:		AAC36804.1	intermediate conductance calcium-activated potassium channel	607	e-173
1			AAC23541.1	hIK1	607	e-173
		·	AAC51913.1	intermediate conductance calcium-activated potassium channel	607	L
• •			AAG26917.1	intermediate-conductance calcium-activated potassium channel 1	. 607	e-173
;; ;;		. 2 · . * <del>*</del> . *	AAH15337.1	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	. 607	. e-173
	· ·		AAK81862.1	AF395661 1 potassium intermediate/small conductance calcium-activated channel, subfamily $\overline{N}$ , member 4	909	
			AAL10706.1	small-conductance calcium-activated potassium channel SK3	286	
	. :		NP_002240.2	small conductance calcium-activated potassium channel protein 3 isoform a	285	1e-76
:			Q9UGI6	KCN3_HUMAN Small conductance calcium-activated potassium channel protein 3 (SK3) (SKCa3)	285	1e-76
			CAB61331.1	SK3 protein	285	1e-76
·			AAK15345.1	AF336797_1 small-conductance calcium-activated potassium channel	285	1e-76
	•		T09172:	probable calcium-activated potassium channel KCNN3	282	1e-75
	*:		AAC26099.1	calcium-activated potassium channel	282	1e-75
	i : ;		092952	KCN1_HUMAN Small conductance calcium-activated potassium channel protein 1 (SK1)	278	2e-75
	: : A	·	AAB09562.1	small-conductance, calcium-activated potassium channel SK1	278	2e-75
	:		AAD37507.1.	small-conductance calcium-activated potassium channel 1	278	. 2e-75
		•	NP 002239.2	small conductance calcium-activated potassium channel protein 1	278	2e-75
			AAK84039.1	AF397175_1 small-conductance calcium-activated potassium channel	280	5e-75
			Q9H2S1	KCN2_HUMAN Small conductance calcium-activated potassium channel protein 2 (SK2)	279	7e-75
			AAG16728.1	AF239613 1 apamin-sensitive small-conductance Ca2+-activated potassium channel	279	7e-75
·.		:	NP 067627.2	small conductance calcium-activated potassium channel protein 2 isoform a; apamin-sensitive small-conductance Ca2+-activated potassium channel	279	7e-75

5 1e-67	5 1e-67	5 1e-67			2 8e-67	2 8e-67	2 8e-67	2 8e-67	2 8e-67	3e-90	0 3e-90		06-99 6	7 2e-89	8 2e-72	7 4e-72	7 4e-72	7 4e-72	7 4e-72	7 4e-72	5 2e-7 <u>1</u>
255	255	255	255	255	252	252	252	. 252	252	330	330	330	329	. 327	268	267	267	267	267	267	265
T-cell surface glycoprotein CD2 precursor	T-cell surface antigen CD2 precursor	T11 surface antigen	d1655N15.1 (CD2 antigen (p50), sheep red blood cell receptor)	CD2 surface antigen	CD2 antigen (p50), sheep red blood cell receptor; lymphocyte-function antigen-2	CD2_HUMAN T-cell surface antigen CD2 precursor (T-cell surface antigen T11/Leu-5) (LFA-2) (LFA-3 receptor) (Brythrocyte receptor) (Rosette receptor)	surface antigen CD2 precursor.	T-cell surface antigen	CD2 antigen (p50), sheep red blood cell receptor ` "	leucine-rich alpha-2-glycoprotein	A2GL_HUMAN Leucine-rich alpha-2-glycoprotein precursor (LRG)	AF403428_1 leucine-rich alpha-2-glycoprotein	lencine-rich alpha-2-glycoprotein	leucine-rich alpha-2-glycoprotein	cytochrome P450	cytochrome P450, subfamily IVA, polypeptide 11; fatty acid omega-hydroxylase; P450HL-omega, alkane-1 monooxygenase; lauric acid omega-hydroxylase	fatty acid omega-hydroxylase (BC 1.14.15) cytochrome P450 4A11	fatty acid omega-hydroxylase; CYP4A11	fatty acid omega-hydroxylase (BC 1.14.15) cytochrome P450 4A11	fatty acid omega-hydroxylase; CYP4A11v	CP4Y_HUMAN Cytochrome P450 4A11 precursor (CYPIVA11) (Fatty acid omega-hydroxylase) (P-450 HK omega) (Lauric acid omega-hydroxylase) (CYP4AII) [P450,HI _nnmen]
RWHUC2	ÅAA35571.1	AAA53095.1	CAC14840.1	AAA51946.1	NP_001758.1	P06729	AAA51738.1	CAA30721.1	AAH33583.1	NP_443204.1	P02750 · ·	AAK05527.1	NBHUA2	AAH34389.1	CAA50586.1	NP_000769.1	I53015	AAB29502.1	165981	AAB29503.1	Q02928
	·	•				· .		:		U:(C-D) 2.06	·	:			U:(C-D) 2.06				•	Ì	
Mm.2284 U:(C-D) 2 2.06	:				·				:	Mm.1769 46					NULL			). (**	` :		
NM_013486 NP_038514.1						1				NM_029796 NP_084072.1			1		X71479 CAA50585.1					· ·	

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:	4.4.		•			
			JX0331	laurate omega-hydroxylase (EC 1.14.15.3) cytochrome P450 4A11 (HL24)	. 265	2e-71
,			AAA58436.1	cytochrome P450	265	2e-71
			BAA05491.1	fatty acids omega-hydroxylase (cytochrome P450HL omega)	265	· 2e-71
		٠	1908216A	fatty acid omega-hydroxylase (cytochrome P450 4A)	265	2e-71
	-		BAA02864.1	fatty acid omega-hydroxylase	265	. 2e-71
			AAF76722.1	AF208532_1 fatty acid omega-hydroxylase CYP4A11	261	2e-70
				dJ18D14.4 (cytochrome P450, subfamily IVA, polypeptide 11)	253	. 6e-68
	1		AAH28102.1	Unknown (protein for MGC:40051)	. 202	1e-52
			BAC05226.1	unnamed protein product	202	1e-52
			BAC03751.1	unnamed protein product	202	1e-52
		U:(C-D)	014753	OVO1_HUMAN Putative transcription factor Ovo-like 1 (hOvo1)	. 468	e-131
NM_019935 NP_064319.1	Mm.3832 3	2.05 U:(IR-D) 2.41	· .			
			NP_004552.1	OVO-like 1 binding protein; putative transcription factor OVO-like 1; ovo (Drosophila) homolog-like 1	367	e-101
			AAB72084.1	OVO-like 1 binding protein	367	e-101
	:		NP_067043.1	zinc finger protein 339; ovo-like 2 (Drosophila)	275	3e-73
			BAB14002.1	unnamed protein product	275	3e-73
			Q9BRP0	Z339_HUMAN Zinc finger protein 339	271	2e-72
1:			AAH06148.1	AAH06148 putative zinc finger protein from EUROIMAGB 566589	271	2e-72
		:	CAB45151.1	hypothetical protein, similar to (AF134804) putative zinc finger transcription factor OVO1 [Mus musculus]	. 238	3e-62
NM_012006 NP_036136.1	Mm.1978	U:(C-D) 2.05	XP_170752.1	similar to peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	602	e-172
	: ''		P49753	PTE2_HUMAN Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	009	e-171
			JC7367	second peroxisomal thioesterase	009	e-171
			AAF97985.1	peroxisomal long-chain acyl-coA thioesterase	909	e-171
			1			

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			AAH04436.1	AAH04436 Unknown (protein for MGC:3983)	000	e-171
		•	AAH06500.1	AAH06500 Unknown (protein for MGC:2366)	009	e-171
			NP_006812.2	peroxisomal long-chain acyl-coA thioesterase; peroxisomal long-chain acyl-coA thioesterase; putative protein	599	e-171
			AAH06335.1	AAH06335 peroxisomal long-chain acyl-coA thioesterase	599	e-171
1				unnamed protein product	598	e-171
			1	hypothetical protein FLJ31235	494	e-139
				umamed protein product	494	e-139
				ORF; putative	405	e-113
			-	similar to Peroxisomal acyl-coenzyme A thioester hydrolase 2 (Peroxisomal long-chain acyl-coA thioesterase 2) (ZAP128)	280	4e-75
			NP 001692.1	bile acid Coenzyme A: amino acid N-acyltransferase; glycine N-choloyltransferase	265	2e-70
			A53965	bile acid-CoA amino acid N-acyltransferase	265	2e-70
	1		AAC37550,1	bile acid CoA; Amino acid N-acyltransferase	265	2e-70
			AAH09567.1	AAH09567 bile acid Coenzyme A: amino acid N-acyltransferase (glycine N-choloyltransferase)	265	2e-70
AK004963	. 1	U.(C-D)				
BAB23703.1	Mm.186	2.04	NP_055419.1	Tax interaction protein 1	243	. 4e-64
·			AAB84248.2	Tax interaction protein 1	243	46-64
1.4			AAG44368.1	AF234997_1 glutaminase-interacting protein 3	243	46-64
• :			AAK69111.1	AF277318 1 tax-interacting protein 1	243	46-64
	;		AAH23980.1	Tax interaction protein 1	243	. 4e-64
			AAF43104.1	TP1	228	2e-59
AK008849	: ·					
BAB25928.1	Mm.45435	0:(C_D) 2.04	NP_079119.2	duodenal cytochrome b; hypothetical protein FLJ23462	391	e-109
			CAB66628.1	hypothetical protein	391	e-109
•			BAB15661.1	unnamed protein product	386	e-107
		!				

			XP_166224.2	similar to data source:SPTR, source key:Q9H0Q8, evidence:ISS-homolog to HYPOTHETICAL 31.6 KDA PROTEIN-putative	196	68-50
			NP_705839.1	hypothetical protein MGC20446	196	6e-50
: ,			BAC11698.1	unnamed protein product	196	6e-50
NM_008532 NP_032558.1	Mm.4259	U.(C-D) 2.03	P16422	TTD1_HUMAN Tumor-associated calcium signal transducer 1 precursor (Major gastrointestinal tumor-associated protein GA733-2) (Epithelial cell surface antigen) (Epithelial glycoprotein) (EGP) (Adenocarcinoma-associated antigen) (KSA) (KS 1/4 antigen) (Cell surface glycoprotein Trop-1)	446	- 124
• !			CAA32870.1	KSA preproantigen peptide	446	e-125
•			AAA36151.1	adenocarcinoma-associated antigen precursor (KSA)	446	e-125
•		:	AAA59543.1	KS1/4 antigen	. 446	e-125
			NP_002345.1	tumor-associated calcium signal transducer 1 precursor; membrane component, chromosome 4, surface marker (35kD glycoprotein); MK-1 antigen; antigen identified by monoclonal antibody AUA1	446	. e-125
;			B48149	epithelial glycoprotein antigen GA733-2 precurso	446	e-125
·. :			AAA35861.1	carcinoma-associated antigen GA733-2	446	è-125
:		?. :	AAB00775.1	carcinoma-associated antigen GA733-2	446	e-125
:			AAH14785.1	tumor-associated calcium signal transducer 1	446	e-125
			AAA35723.1	epithelial glycoprotein (EGP) precursor	444	e-124
	: ;	•	A48149	carcinoma-associated antigen GA733-1 precursor	265	2e-70
	•	· · ·	CAA31781.1	GA733-1 protein (AA 1-323)	265	2e-70
		•	CAA54801.1	gp50/TROP-2	265	2e-70
			AAH09409.1	Unknown (protein for MGC:10655)	265	2e-70
	· ,			tumor-associated calcium signal transducer 2 precursor; membrane component, chromosome 1, surface marker 1 (40kD glycoprotein, identified by monoclonal		
			NP_002344.1	antibody GA733); epithelial glycoprotein-1	263	6e-70
			CAA54799.1	gp50/Trop-2	263	6e-70
			P09758	TTD2_HUMAN Tumor-associated calcium signal transducer 2 precursor (Pancreatic carcinoma marker protein GA733-1) (Cell surface glycoprotein Trop-2)	262	1e-69
			AAA52505.1	GA733-1 protein precursor	. 262	1e-69

Mm.16106 2.02 P01028 COA HTIM		COA HIMAN Complement of programmer Contained CAA careed and an annual and a careed	0	. (
	1	complement C4A precursor [validated]	2586	
AAA51855.1 complement		complement component C4A	2586	0
NP_009224.1 C4;complem		complement component 4A preproprotein; acidic C4; Rodgers form of C4; complement component 4S	2583	0
CAB89302. dJ34F7.4 (c		dJ34F7.4 (complement component 4A)	2582	0
NP_000583.1 complement component 4F	<b>=</b> .	complement component 4B preproprotein; Chido form of C4; basic C4; complement component 4F	2581	0
AAB67980.1 complemen		complement component C4	2581	0
!	-	complement component C4A	2563	0
AAA99717.1 complemen	72	complement C4B precursor	2465	0
NP_000055.1 complement		complement component 3 precursor	624	e-178
P01024 CO3_HUM		CO3_HUMAN Complement C3 precursor	624	e-178
C3HU complement		complement C3 precursor [validated]	624	e-178
AAA85332,1 complement	'	complement component C3	624	e-178
AAA59651.1 complemen	= 1	complement component C4B	573	e-163
1HZF A Chain A	-	A Chain A, C4adg Fragment Of Human Complement Factor C4a	544	e-154
	Ī			
2 NP_000923.1 phospholip:	ਲ ।	phospholipase C, beta 3 (phosphatidylinositol-specific)	2015	. 0
PIP3_HUM Q01970 (PLC-beta-2		PP3_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta 3 (PLC-beta-3) (Phospholipase C-beta-3)	2015	
I38994 phospholipase C-beta-3	. 031	e C-beta-3	2015	0
AAA77683.1 phospholipase C-beta-3		se C-beta-3	2015	0
S52099 phospholip	G I	phospholipase C beta 3	1967	0
CAA85776.1 phospholipase C beta 3		use C beta 3	1967	0
AAH32659.1 Similar to p		Similar to phospholipase C, beta 3	1824	0

			-			
			S27002	phospholipase C (EC 3.1.4.3), phosphatidylinositol-specific	1663	0
			CAA78903.1	phospholipase c	1663	0
	· · · · · · · · · · · · · · · · · · ·			phospholipase C, beta 1 (phosphoinositide-specific); phosphoinositide-specific		
			NP_056007.1	puospuonpase Coeta 1; phospholipase C beta 1; phospholipase C, beta 1(phospholipase C, beta	1197	. 6
			O9NO66	PIB1_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta		
			17	phospholipase C-beta-1a	1197	0
			-	phospholipase C-beta-1b	1102	
		·	1.	phospholipase C beta 1	1154	٥
	· ·	•	BAA25507.	KIAA0581 protein	1047	0
	• • •		NP_004564.1	phospholipase C, beta 2	934	0
	:	,:	Q00722	PIB2_HUMAN 1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase beta 2 (PLC-beta-2) (Phospholipase C-beta-2)	934	6
		<i>.</i> :	A43346	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase (EC 3.1.4.11) beta-2	934	0
			153.1	phospholipase C-beta-2.	934	0
:		• •	T46339	hypothetical protein DKFZp434A0814.1	885	0
		·	CAB70666.1	hypothetical protein	885	0
NM_010129 NP_034259.1	Mm.2082 9	U:(C-D) 2	NP_001416.1	epithelial membrane protein 3	250	1e-66
			P54852	EMP3_HUMAN Epithelial membrane protein-3 (EMP-3) (VMP protein) (Hematopoietic neural membrane protein) (HNMP-1)	250	1e-66
:		:	AAC50920:1	YMP	250	1e-66
			AAC51730.1	hematopoietic neural membrane protein	250	1e-66
			AAH09718.1	AAH09718 epithelial membrane protein 3	.250	1e-66
		.:	JC5045	epithelial membrane protein 3	244	66-65
. 1			CAA64394.1	epithelial membrane protein-3	244	6e-65
NM_011644 NP_035774.1	Mm.8361 5	U:(C-D) 2	NP_004612.2	transient receptor potential cation channel, subfamily C, member 6; transient receptor potential channel 6	. 427	e-119
						7

	:		Q9Y210	TRP6 HUMAN Short transient recentor notential channel 6 (TmC6)	101	0.110
			CAA06943.1	transient receptor potential protein	127	6 110
	,		AAC63289.2	transient receptor potential protein 6	427	-112 -110
	·		CAC01684.1	transient receptor potential channel 6	427	6-110
			NP_003296.1	transient receptor potential cation channel, subfamily C, member 3; transient receptor potential channel 3	421	e-117
	· .		Q13507	TRP3_HUMAN Short transient receptor potential channel 3 (TrpC3) (Htrp-3) (Htrp3)	421	e-117
			CAA74083.1	transient receptor potential related chamel 3 protein	421	e-117
		·	AAC51653.1	calcium influx channel	421	e-117
		;	NP_065122.1	putative capacitative calcium channel	411	e-114
			09НСХ4	TRP7_HUMAN Short transient receptor potential channel 7 (TrpC7) (TRP7 protein)	441	e-114
			CAC03489.1	putative capacitative calcium channel	411	e-114
1	.:		CAD19069.1	short transient receptor potential channel 7	409	e-113
.	·		AAF22928.1	AF063823_1 trp-related protein 4 truncated variant beta	369	e-101
		:	AAL24550.1	AF421359_1 transient receptor potential channel 4 beta splice variant	369	e-101
: -			AAL24551.1	AF421360_1 transient receptor potential channel 4 epsilon splice variant	369	e-101
		;	NP_057263.1	transient receptor potential 4; transient receptor potential chamel 4	369	e-101
			Q9UBN4	TRP4_HUMAN Short transient receptor potential channel 4 (TrpC4) (trp-related protein 4) (hTrp-4) (hTrp4)	369	e-101
		:	AAD51736.1	AF175406_1 transient receptor potential 4	698 .	e-101
			AAF22927.1	AF063822_1 trp-related protein 4	369	e-101
		-	AAL24549,1	AF421358_1 transient receptor potential channel 4 alpha splice variant	369	e-101
. ;			AAF22929.1	1	369	e-101
			NP_036603.1	transient receptor potential cation channel, subfamily C, member 5; transient receptor potential channel 5	359	2e-98
		•	Q9UL62	TRP5_HUMAN Short transient receptor potential channel 5 (TrpC5) (Htrp-5) (Htrp5)	359	2e-98
		•	AAF00002.1	AF054568_1 transient receptor potential calcium channel 5	359	2e-98
			CAC01686.1	transient receptor potential channel 6, variant delta 377-431	333	1e-90
					)	->>>

Subtable 1C: Mixed Genes and Proteins

	- 1					
Mouse Gene Protein	Unigene	Behavior	Human . Proteins	Human Protein Name	Score	E-value
NM 011369	Mrh 37801	11-(C-IR)	NP 079071 2	likely ortholog of monse (The CH2 domain hinding protein 1. himselection) and the	700,	
NP 035499.1		2.88	1	FLJ22009	÷ 001	 >
; I ;		F:(R-D)				
		-7.03			•	
			AAH30699.1	Unknown (protein for MGC:26900)	1004 0	0
		. 3	BAB71049.1	unnamed protein product	1003 0	. 0
		·	XP_015700.2	similar to Shc SH2-domain binding protein 1	632	0
			BAB15208.1	unnamed protein product	630	630 e-180
:			AAH00960.1	AAH00960 Unknown (protein for IMAGE:3451160)	615	e-176
			AAG45336.1	GE36	230	8E-60
		,	NP_112195.1	chromosome 1 open reading frame 14; GB36 gene	228	2E-59
			AAG60617.1	AF288398_1 Clorf14	228	2B-59
			AAG60616.1	AF288397 1 Clorf14	204	204 6E-52
NM 015810	Mm.859	U.(C-IR)	Q9UHN1	DPG2 HUMAN DNA polymerase gamma subunit 2, mitochondrial precursor	712	.0
INF_030023.1		2./4		(Mitochondrial DINA polymerase accessory subunit) (PolG-beta) (MtPolB) (DINA		,
	·. :	F:(IR-D)  -3.23		polymerase gamma accessory 55 kDa subunit) (p55)		
			AAD50382.1	AF142992 1 DNA polymerase gamma accessory subunit	712	0
1.11.12 10 11	•		AAD56640.1	AF177201 1 mitochondrial DNA polymerase accessory subunit precursor	7110	0
·		÷	AAH09194.1	AAH09194 Unknown (protein for MGC:15231)	7100	0
	• • •		AAD56542.1	AF184344 1 DNA polymerase accessory subunit precursor	707	0
		: .	NP_009146.1	polymerase (DNA directed), gamma 2, accessory subunit; mitochondrial DNA polymerase, accessory subunit	009	600 e-171
· · ·			AAC51321.1	mitochondrial DNA polymerase accessory subunit precursor	009	e-171
			1			
NM_007659	Mm.4761	U:(C-IR)	NP_001777.1	cell division cycle 2 protein, isoform 1; cell division control protein 2 homolog;	577	577 e-164
NP 031685.1		F:(TR-D)	: :	cycun-dependent triase 1; po4 protein triase; cell cycle controller CDC2	•	
	•	-2.86 ʻ				•
; ; ;			P06493	CDC2 HUMAN Cell division control protein 2 homolog (p34 protein kinase)	577	577 e-164
	.  .					

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9 164	e-164	e-164	e-164	577 e-164	e-164	e-114	e-114 ·	e-109	393 e-109	393 e-109	e-109	e-108	e-108	e-108	A-108	e-108 ·	389 e-108	389 e-108	e-108	e-108	e-108	389 e-108
577	577		577	577	577	409	409	393	393	393	393	390	389	380	380	389	389	389	389	389	389	389
protein kinase (EC 2.7.1.37) ede.	CDC2 polypeptide (CDC2) (AA 1-297)	CDC2 protein (AA 1-297)	Similar to cell division cycle 2, G1 to S and G2 to M	AF512554_1 cell division cycle 2, G1 to S and G2 to M	gene CDC2		CDC2 delta T	cyclin-dependent kinase 3	CDK3_HUMAN Cell division protein kinase 3	protein kinase (EC 2.7.1.37) cdk	serine/threonine protein kinase [Homo sapiens]	cell division kinase. CDC2 homolog	cyclin-dependent kinase 2, isoform 1; cdc2-related protein kinase; cell devision kinase 2: p33 protein kinase	CDK2_HUMAN Cell division protein kinase 2 (p33 protein kinase)	protein kinase (EC 2.7.1.37) cdk2	A Chain A, Cdk2 Complexed With N-Methyl-4-{[(2-0xo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}benzenesulfonamide	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With N-Methyl- {4-[2-(7-Oxo-6,7-Dihydro-8h-[1,3]thiazolo[5,4-B]indol-8. Ylidene)hydrazinolphenyl}methanesulfonamide	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-{[(2,2-Dioxido-1, 3-Dihydro-2-Benzothien-5-Y])amino]methylene}-5-(1,3-Oxazol-5-Y])-1,3-Dihydro-2h-Indol-2-One	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 4-{[(2-Oxo-1,2-Dihydro-3h-Indol-3-Ylidene)methyl]amino}-N-(1,3-Thiazol-2-Yl)benzenesulfonamide	A Chain A, Cyclin-Dependent Kinase 2 (Cdk2) Complexed With 3-{[4-([amino(Imino)methyl]aminosulfonyl)anilino]methylene}- 2- Oxo-2,3-Dihydro-1h-Indole	A Chain A, Cyclin A - Cyclin-Dependent Kinase 2 Complex	C Chain C, Cyclin A - Cyclin-Dependent Kinase 2 Complex
A29539	CAA28963.1	CAA68376.1	AAH14563.1	AAM34793.	1306392A	NP_203698.1	BAA26001.1	NP_001249.1	Q00526	S23382	CAA47001.1	CAA43807.1	NP_001789.2	P24941	A41227	1KES	1KE6	IKE7	1KB8	1KE9	1FIN	1FIN
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389 e-108	389 e-108	389 6-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	-389 e-108	389 e-108	389 e-108	389 e-108	389 e-108	389 6-108	389 e-108	389 e-108	389 e-108
C Chain C, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	A Chain A, The Structure Of Cdk2CYCLIN A IN COMPLEX WITH AN OXINDOLE Inhibitor	Human Cyclin-Dependent Kinase 2	Human Cyclin-Dependent Kinase 2	A Chain A, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	A Chain A, Crystal Structure Of The Human Cdk2 Kinase Complex With Cell Cycle-Regulatory Protein Ckshs1	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4- [(6-Amino-4-Pyrimidinyl) AminoTbenzenesulfonamide	P Chain P, Crystal Structure Of Human Cdk2 (Unphosphotylated) In Complex With Pkf049-365	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With 4-[3-Hydroxyanilino]-6,7-Dimethoxyquinazoline	A Chain A, The Structure Of Cyclin-Dependent Kinase 2 (Cdk2) In Complex With An Oxindole Inhibitor.	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Purvalanol B	Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Staurosporine	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Cdk4 Inhibitor	A Chain A, Crystal Structure Of Human Cyclin Dependent Kinase 2 (Cdk2) In Complex With The Inhibitor H717	A Chain A, Human Cyclin-Dependent Kinase 2 Complexed With The Inhibitor Hymenialdisine	C Chain C, Crystal Structure Of Murine Gamma Herpesvirus Cyclin Complexed To Human Cyclin Dependent Kinase 2	cdc2-related protein kinase	cyclin-dependent kinase 2.	AF512553_1 cyclin-dependent kinase 2	cyclin A dependent p33 kinase:SUBUNIT=2
1FVV.	1FVV	1HCL	1HCK	1F5Q	1BUH	1JSV	1JVP	1DI8	IFVT	1CKP	1401	1GIE	1G5S .	1DM2	1F5Q	AAA35667.1	AAH03065.1	AAM34794.1	1717387A
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389 e-108	389 e-108	389 e-108	389 e-108	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107	387 e-107.	636 0
A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu6027	A Chain A, Human Cyclin Dependent Kinase 2 Complexed With The Inhibitor Nu2058	A Chain A, Human Cyclin-Dependent Kinase 2	A Chain A, Human Cyclin-Dependent Kinase 2 Phosphorylated On Thr 160	C Chain C, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	A Chain A, Thr 160 Phosphorylated Cdk2 - Human Cyclin A3 Complex With The Inhibitor Indirubin-5-Sulphonate Bound	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu2058	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6094	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6086	A Chain A, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	C Chain C, Structure Of Human Thr160-Phospho Cdk2CYCLIN A COMPLEXED With The Inhibitor Nu6102	A Chain A, Pedk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	C Chain C, Pcdk2CYCLIN A IN COMPLEX WITH MGADP, NITRATE AND PEPTIDE Substrate	A Chain A, Phosphorylated Cdk2-Cyclyin A-Substrate Peptide Complex	C Chain C, Phosphorylated Cdt/2-Cyclyin A-Substrate Peptide Complex	cdk2	A2AC_HUMAN Alpha-2C-adrenergic receptor (Alpha-2C adrenoceptor) (Subtype C4) .
ıBıx	1E1V .	1B38	1B39	1E9H	1E9H	IHIP	IHIP	1H1Q	1H1Q	1H1R	IHIR	1H1S	1H1S	1GY3	1GY3	1QMZ	10MZ	CAA43985.1	P18825
					:			· ·					  	\		·			U:(C-IR) 2.41
·			:.		:	:	**  :			1. 1.	, , ,								Mm.57205
							: .						: 4			· X	**		NM_007418

•		636 0		634 0	601 e-171	601 6-171	601 e-171	601 8-171		385 e-106	· 384 e-106		384 e-106	384 P-106	384 106	384 6-106	384 P-106	387 8-105	381 e-105	358 2E-98	355 2E-97	355 2P-07	258 4F-68	258 4E-68	258 4E-68	764 0	·			7640
		AF280399 1 alpha 2C adrenergic receptor	alpha2CII-adrenergic receptor	AF280400 1 alpha 2C adrenergic receptor variant	alpha-2C-adrenergic receptor; alpha2-AR-C4	alpha-2C-adrenergic receptor	kidney alpha-2-adrenergic receptor	alpha2-C4-adrenergic receptor	alpha-2A-adrenergic receptor			adrenoceptor; alpha-2AAR subtype C10	A2AA_HUMAN Alpha-2A adrenergic receptor (Alpha-2A adrenoceptor) (Alpha-2AAR subtype C10)	AF281308 1 alpha 2A adrenergic receptor	adrenergic receptor alpha-2A	alpha-2A adrenergic receptor	alpha-2A adrenergic receptor	AF316894 1 alpha 2A adrenergic receptor	alpha-2-adrenergic receptor old gene name 'ADRA2R'.	AF316895 1 alpha 2B adrenergic receptor	A2AB_HUMAN Alpha-2B adrenergic receptor (Alpha-2B adrenoceptor) (Subtype C2)	alpha2B-adrenergic receptor	alpha-2B-adrenergic receptor; alpha-2-adrenergic receptor-like 1	alpha-2B-adrenergic receptor	alpha-2-adrenergic receptor (alpha-2 C2) old gene name 'ADRA2RL1'			1		similar to actin. alpha cardiac
		AAG28076.1	BAA02737.1	AAG28077.1	NP 000674.1	A31237	AAA35513.1	AAC78723.1	A34169	AAA51665.1	NP_000672.2		P08913	AAF91441.1	AAG00447.2	AAK26743.1	AAK51162.1	AAK01634.1	A:AA51664.1	AAK01635.1	P18089	AAB62558.1	NP 000673.1	A37223	AAA51666.1	NP_005150.1				XP 012405.3
	F:(IR-D) -2.1																		,		,	;				U:(C-IR)	F:(C-D) -	2.42	F:(TR-D) -5.6	
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	NP_031444.1	,									1		·: , ,		·						·					NIM_009608	NP_033738.1			

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764		10/	/04 0	764	759 0	759 10		759		759		759 0	759 0	755	755	755 0	755 0	752	752 0	7500	750 0	750 0	750	750	750 0	723 0	723 0	723 0	723 0	723	723	723 0	723 0	723 0
ACTC HUMAN Actin alpha cardiac	actin cardiac muscle	of tale and discontinuous	appe variate aciti	AAH09978 actin, alpha, cardiac muscle	alpha 1 actin precursor; alpha skeletal muscle actin	similar to Chain B, The X-Ray Crystal Structure Of The Complex Between Rabbit	Skeletal Muscle Actin And Latrunculin A At 2.85 A Resolution	ACTS_HUMAN Actin, alpha skelefal muscle (Alpha-actin 1)	actin alpha 1, skeletal muscle	alpha-actin	alpha-skeletal actin precursor	AF182035 1 skeletal muscle alpha-actin precursor	Similar to actin, alpha 1, skeletal muscle	alpha 2 actin; alpha-cardiac actin	ACTA HUMAN Actin, aortic smooth muscle (Alpha-actin 2)	alpha-actin (AA 1-377)	AAH17554 actin, alpha 2, smooth muscle, aorta	actin alpha 2, aortic smooth muscle	alpha-actin	actin, gamma 2 propeptide; actin, alpha-3	ACIH HUMAN Actin, gamma-enteric smooth muscle (Alpha-actin 3)	actin gamma, enteric smooth muscle	gamma-actin (AA 1-376)	enteric smooth muscle gamma-actin	Similar to actin, gamma 2, smooth muscle, enteric	gamma-actin	actin, gamma 1 propeptide; cytoskeletal gamma-actin; actin, cytoplasmic 2	ACTG HUMAN Actin, cytoplasmic 2 (Gamma-actin)	actin gamma 1	gamma-actin	gamma-actin .	actin, gamma 1	actin, gamma 1	actin, gamma 1
P04270	ATHUC	A A D 50,610 1	1.61066000	AAH09978.1	NP 001091.1	XP_001869.1		P02568	ATHU	AAB59376.1	AAA60296.1	AAF02694.1	AAH12597.1	NP:001604.1	P03996	CAA32064.1	AAH17554.1	ATHUSM	AAA51577.1	NP 001606.1	P12718	A40261:	CAÄ34814.1	BAA00546.1	AAH12617.1	JC5818	NP 001605.1	P02571	ATHUG	CAA27723.1	AAA51579.1	AAH00292.1	AAH01920.1	AAH07442.1
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		Similar to actin, gamma 1	Similar to actin, gamma 1	actin, gamma 1	actin, gamma 1	actin, gamma 1	actin, gamma 1	beta actin; beta cytoskeletal actin	ACTB_HUMAN Actin, cytoplasmic 1 (Beta-actin)	beta	ctin	cytoplasmic beta actin	beta	beta	beta	beta	beta	beta	beta	mutant beta-actin (beta'-actin)	chromosome 21 open reading frame 33; human HESI protein, homolog to E.coli and	Zeoransh est protein	HUMAN BS1 protein homolog, mitochondrial precursor (Protein KNP-I)	(GT335 protein)	anti-sigma cross-reacting protein homolog I alpha precursor	Ia		similar to E. coli SCRP27A and to zebrafish ES1	ES1 (zebrafish) protein, human homolog of	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	EST (Zeoranish) protein, munan nomorog or
A ATTORON TO A		•		AAH15005.1 actin		AAH15779.1 actin			•	ATHUB actin beta	CAA25099.1 beta-actin	AAA51567.1 - cytog	AAH01301.1 actin, beta	AAH02409.1 actin, beta	AAH04251.1 actin, beta	AAH09275.1 actin, beta	AAH13380.1 actin, beta		AAH16045 actin, beta	CAA'45026.1 muta	NP_004640.1 chro	76017 	P30042 ES1	. (GT	JC4913 anti-	1	AAC50938.1 GT335		AAH02370.1 ES1	A A HA 1 1001	
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						i de de la compansión d										•		:.	:		AA510875 N	NP_613067.1		,	:					:	1

			-	TABLE		
			BAA21138.1	KNY-1 alpha protem	243	243 9E-65
	:					
NM_009349	Mm.299	F:(C-IR) -2.85	AAD04723.1	thioether S-methyltransferase-like; similar to P40936 (PID:g731019)	271	271 9B-73
NP_033375.1		U:(IR-D) 3.02				
}-			0950560	INMIT_HUMAN Indolethylamine N-methyltransferase (Aromatic alkylamine N-	267	2E-71
		•	:	methyltransferase) (Indolamine N-methyltransferase)(Arylamine N-methyltransferase) (Amine N-methyltransferase)		
,						
	: .	٠.	AAF18304.1	AF128846 1 indolethylamine N-methyltransferase	267	2E-71
•		·	AAF18306.1	AF128848 1 indolethylamine N-methyltransferase	267	267 2E-71
•	,		NP 006765.3	indolethylamine N-methyltransferase; thioester S-methyltransferase-like	266	266 5E-71
			AAF18305.1	AF128847 1 indolethylamine N-methyltransferase	266	266 5E-71
	• •		AAH33813.	Unknown (protein for IMAGE:5209218)	. 266	266 5E-71
:		:	60.1	nicotinamide N-methyltransferase	239	6E-63
			1	NNMT_HUMAN Nicotinamide N-methyltransferase	239	6B-63.
		·	A54060	nicotinamide N-methyltransferase (BC 2.1.1.1)	. 239	239 GE-63
, ,		•	AAA19904.1	nicotinamide N-methyltransferase	239	239 GE-63
	•		AAA93158.1	nicotinamide N-methyltransferase	239	239 GE-63
			AAH00234.1	AAH00234 nicotinamide N-methyltransferase	235	239 GE-63
NM 019813 NP 062787.1	Mm.19016 F:(C-IR)	_ •	Q16643	DREB_HUMAN Drebrin (Developmentally regulated brain protein)	0 09/	. 0
		U:(IR-D)	:. ,			
		2.42				
			9080NC	drebrin E (clone gDbh13)	260	0
•		î	AAA16256.1	drebrin B2	0 09/	0
	.;		BAA04480.1	drebrin E	0 09/	
Y	; ::		AAH00283.1	AAH00283 drebrin 1	. 760 0	
			AAH07281.1	AAH07281 drebrin 1.	760	0
	! :			AAH07567 drebrin 1	760	0
			NP 004386.2	drebrin 1 isoform a; drebrin B; drebrin-1; drebrin B2	759	0
			T14763	hypothetical protein DKFZp434D064.1	704 0	
	:		-	hypothetical protein	704 0	0
		:	NP 543157.1	drebrin 1 isoform b; drebrin B; drebrin-1; drebrin B2	703 0	. 0

1749 0		1749 0	1749 0	1749 0	741 0	630 e-180		628 e-179	628 e-179	628 e-179	628 e-179	623 e-178	623 e-178	499 e-140	499 e-140	498 e-140	498 e-140
1 TAL1 (SCL) interrupting locus; SCL interrupting locus		SIL protein	SIL	SIL protein	dJ18D14.1 (TAL1 (SCL) interrupting locus )	S-adenosylmethionine decarboxylase 1		S-adenosylmethionine decarboxylase 1 precursor	DCAM_HUMAN S-adenosylmethionine decarboxylase proenzyme (AdoMetDC) (SamDC) [Contains: S-adenosylmethionine decarboxylase alpha chain; S-adenosylmethionine decarboxylase beta chain]	adenosylmethionine decarboxylase (BC 4.1.1.50) precursor	S-adenosylmethionine decarboxylase proenzyme (EC 4.1.1.50) old gene name 'AMD'	B Chain B, Structure Of A Human S-Adenosylmethionine Decarboxylase Self- Processing Ester Intermediate And Mechanism Of Putrescine Stimulation Of Processing As Revealed By The H243a Mutant	A Chain A, Structure Of A Human S-Adenosylmethionine Decarboxylase Self- Processing Ester Intermediate And Mechanism Of Putrescine Stirmulation Of Processing As Revealed By The H243a Mutant	A Chain A, Human S-Adenosylmethionine Decarboxylase	C Chain C, Human S-Adenosylmethionine Decarboxylase	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With Methylglyoxal Bis- (Guanylhydrazone)	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound 5'-Deoxy-5'-[n- Methyl-N-(2-Aminooxyethyl) Amino]adenosine
NP_003026.1		A41685 ·	AAA60550.1	AAK51418.1	CAB72102.1	AAH00171.1		NP 001625.1	P17707	DCHUDM	AAA51716.1	1JL0	1JL0	1JEN	1JEN	117C	1172
F:(C-IR) -2.64	U:(IR-D) 2.51					F:(C-IR)	-2.6 U:(IR-D) 3.96				·			·			
					:	Mm.7880											
NM_009185 Mm 3988	NF_033211.1					NM_009665	NP_033795.1										

			·		276_	·	_	 			_			_							
498 e-140	498 e-140	474 e-133	474 e-133	201 2E-51.		201 2E-51	201 2E-51	0 089		:	0 089	0 089	0 9/9	.0 9/9	362 1E-99	301 2E-81	301 2E-81		301 2E-81	301 2E-81	296 5E-80
4.	4 .	4	4	72		2	2(	9			9	9	9	9	æ	ñ	Ğ.	_	3(	3	2
A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyriuvoyl Group And Covalently Bound 5'-Deoxy-5'-[(3-Hydrazinopropyl)methylamino]adenosine	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Covalently Bound S-Adenosylmethionine Methyl Ester	A Chain A, Human S-Adenosylmethionine Decarboxylase With Covalently One-2'-Amidinohydrazone	C Chain C, Human S-Adenosylmethionine Decarboxylase With Covalently Bound Pyruvoyl Group And Complexed With 4-Amidinoindan-1-One-2'-Amidinohydrazone	KIAA1749 protein		hypothetical protein FLJ14957	unnamed protein product	wingless-type MMTV integration site family, member 11 precursor			WN11 HUMAN WNT-11 protein precursor	WNT11	WNT11	HWNT1	unnamed protein product	WNT4	wingless-type MMTV integration site family, member 4 precursor; signaling protein	WNT-4; WNT-4 protein precursor	WNT4 HUMAN WNT4 protein precursor	AF316543 1 signaling protein WNT-4	WNT4 precursor
1179	1I7B	117М	117M	BAB21840.1		NP 116255.1	BAB55415.1	NP_004617.2			096014	BAB72099.1	CAA73223.1.	CAA74159.1	BAC11683.1	BAC23080.1	NP_110388.2		P56705	AAK51699.1	AAG38658.1
			, , , , , , , , , , , , , , , , , , ,	F:(C-IR)	-2.43 U:(IR-D) 2.5			 F.(C-IR)	-2.4 U:(C-D) 2.09	U:(IR-D) 2.84			· ;						:		
				Mm.87428 F:(C-IR				Mm.22182	i : : : : : : : : : : : : : : : : : : :			•					::				
				NM_026599 NP_0808751	101 0000 1011			 NM_009519	NP_033545.1		::				·	•		:			

		<u>.</u>								27	7										_	_			
5 1B-79	262 1E-69	262 1E-69	2 1E-69	262 1E-69	262 1E-69	261 3E-69	261 3E-69	261 3E-69	1 3E-69	5 1E-67	1030 0			1030 0	1030 0	· ·	0 08	1030 0	1030 0	1030 0	1030 0	1028 0	1028 0	1005 0	0 669
295	26	26	. 262	26	26	. 26	26	26	261	255	103	,		103	10		1030	10.	10	위	2	2	01	10	9
Id1224A6.2 (similar to Mouse Wnt-4 protein)	1	+	WN5B HUMAN WNT-5B protein precursor	AAH01749 Similar to wingless-related MMTV integration site 5B			WN5A HUMAN WNT-5A protein precursor	proto-oncogene Wnt-5A precursor		WNT5b precursor				similar to 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (6PF-2-K/Fru-2,6-P2ASB brain/olacenta-type isozyme) (iPFK-2)	F263_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (6PF-2-	K/Fru-2, 6-P2ASB brain/placenta-type isozyme) (iPFK-2) [Includes: 0-phosphoructo-2-kinase : Fructose-2, 6-bisphosphatase ]	1_			_		-		T	T_
CAR526011	NP_116031.1	NP_110402.2	O9H1J7	AAH01749.1	BAB62039.1	NP_003383.1	P41221	A489,14	AAA16842.1	AAG38659.1	NP 004557.1		•.	XP_096349.2	Q16875		BAA08624.1	AAD08818.1	AAL#0083.1	AAH40482.	2208342A	AAB99795.	JC4626	AAC62000	CAA06605.
									· ·		F:(C-IR)		U:(TR-D)			:									
											Mm.19669	:	. ·			•							1		
											AF294617		AAG02118.1									:			

. 0 /69	0 889	0 889	0 089	·0 089	0 0/9	.0 029	0 029	0 0/9	. 670 0	0 699	910 0	•			910 0	773 0	. 609 e-173	609 e-173	609 e-173	609	609 6-173	609 0-173
F262_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2 (6PF-2-K/Fru-2,6-P2ASB heart-type isozyme) (PFK-2/FBPase-2) [Includes: 6-phosphofructo-2-kinase; Fructose-2,6-bisphosphatase ]	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2; Fructose-2,6-bisphosphatase, cardiac isozyme	6-phosphofructo-2-kinase	6-phosphofructo-2-kinase heart isoform	AF470623 1 PFK2/F26DPase	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	F264_HUMAN 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (6PF-2-K/Fru-2,6-P2ASE testis-type isozyme) [Includes: 6-phosphofructo-2-kinase; Fructose-2,6-bisphosphatase]	6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase	testis 6-phosphofructo-2-kinase/fructose 2,6-bisphosphatase	AAH10269 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	6-phosphofructo-2-kinase (EC 2.7.1.105) / fructose-2, 6-bisphosphate 2-phosphatase (EC 3.1.3.46	cyclic nucleotide gated channel beta 3; cyclic nucleotide-gated chanel, beta 3				AF272900_1 cone photoreceptor cyclic nucleotide-gated channel beta subunit	AF228520 1 cone photoreceptor cGMP-gated cation channel beta-subunit	CNG4_HUMAN Cyclic-nucleotide-gated cation channel 4 (CNG channel 4) (CNG-4) (CNG4) (Cyclic nucleotide-gated cation channel modulatory subunit)	cyclic nucleotide-gated cation channel	cGMP-gated cation channel 2, rod	cGMP-gated cation channel subunit 2, cGMP-gated cation channel, subunit beta, hRCNC2 [human, retinal rod cells, Peptide, 909 aa]	cyclic nucleotide-gated cation chamel	cGMP-gated cation channel beta subunit
060825	NP_006203.1	CAA06606.1	BAB19681.1	AAL99386.1	NP 004558.1	Q16877	BAA18921.1	AAD09427.1	AAH10269.1	JC5871	NP_061971.2				AAF86274.1	AAF80179.1	Q14028	AAA65620.1	S32538	AAB32607.1	1912307A	AAB63387.1
		1.		į						· }:	F:(C-IR)	-2.33 U:(C-D)	3.63	0:(IK-D) 2.84	·						· · ·	:
· 1								::			Mm.10357	; , .						;				
					:					· .i		NF_038955,1			.,					: 1:		

						,
			NP_001288.1	cyclic nucleotide gated channel beta 1; cyclic nucleotide gated channel (photoreceptor), cGMP gated 3 (gamma)-like	600	609 e-173
			A A C04830.1	rod photoreceptor CNG-channel beta subunit	609	e-173
			T	cyclic moleotide-pated cation channel	865	598 e-170
,			T	cyclic nucleotide-pated channel protein	269	3E-71
			7	cyclic nucleotide gated channel alpha 3	269	269 3E-71
			Q16281	CNG3 HUMAN Cyclic-nucleotide-gated cation channel alpha 3 (CNG channel alpha	269	269 3E-71
				3) (CNG-3) (CNG3) (Cyclic nucleotide gated channel alpha 3) Cone photoreceptor (GMP-gated channel alpha subunit)		
			AAC17440.1	cone photoreceptor cGMP-gated channel alpha subunit	269	3E-71
·			NP 000078.1	cyclic nucleotide gated channel alpha 1	268	268 GE-71
		-	A42161	cGMP-gated cation channel, rod photoreceptor	268	GB-71
<u>.</u>		٠.	AAA52010.1	cGMP-gated cation channel protein	268	6E-71
NM_026302	Mm.78718 F:(C-IR)		NP_057305.1	dynactin 4 (p62); dynactin p62 subunit	886	
		U:(IR-D)	,			
			XP 041993.1	similar to dynactin 4 (p62); dynactin p62 subunit	886 0	0
			AAF03896.1	AF195120 1 dynactin p62 subunit	0 988	0
			BAA91066.1		886 0	. 0
	:		AAH26323.1	dynactin 4 (p62)	883 0	0
			T47143	hypothetical protein DKFZp7611032.1	282	8E-76
			CAB82417.1	hypothetical protein	282	8E-76
					-	
NM_007755	Mm.22062	F:(C-IR) -2.2	NP_085097.2	cytoplasmic polyadenylation element binding protein; hypothetical protein FLJ13203 similar to cytoplasmic polyadenylation element binding protein; cytoplasmic	1039 0	0
NP_031781.1	:	U:(TR-D) 2.11		polyadenylation element-binding protein		
			AAK01239.1	AF329402_1 cytoplasmic polyadenylation element-binding protein long form	1039 0	. 0
			AAK01240.1	AF329403_1 cytoplasmic polyadenylation element-binding protein short form	868	0
			AAH35348.1	Similar to cytoplasmic polyadenylation element binding protein	. 880	0
			BAB14496.1	unnamed protein product	878	. 0
			NP 055727.1	KIAA0940 protein	20.	207 SE-53
			NP 055727.1	KIAA0940 protein		207

			BAA76784.1	KIAA0940 protein	207	207 SE-53
			1	similar to RIKEN cDNA 4930447D24	207	207 6E-53
			•	KIAA1673 protein	207	207 6E-53
			AAH36899.1	Unknown (protein for MGC:46609)	207	6E-53
		ŀ	_	Similar to KIAA0940 protein	203	9E-52
NM_008422	Mm.39092 F:(C-IR)	Г	<u></u>	Shaw-related voltage-gated potassium channel protein 3; Kv3.3; voltage-gated	0 8//	. 0
	-2			potassium channel protein KV3.3		
NP_032448.1	<u>, c</u>	U:(C-D)				
	<u> </u>	U:(IR-D) 2.33			٠.	
			Q14003	KNC3_HUMAN Potassium voltage-gated channel subfamily C member 3 (Potassium channel Kv3.3) (KSHIIID)	778	0
			AAC24118.1	Shaw type potassium channel Kv3.3	778 0	0
				Shaw-related voltage-gated potassum channel protein 1; voltage-gated potassium channel protein KV3.1; potassium voltage-gated channel subfamily C member 1	612	612 e-175
,			P48547	KNC1_HUMAN Potassium voltage-gated channel subfamily C member 1 (Potassium channel Kv3.1) (Kv4) (NGK2)	612	612 e-175
			A46020	potassium channel KCNC1	612	e-175
			AAB25764.1	voltage-gated potassium channel; NGK2	612	612 e-175
			NP_004969.2	Shaw-related voltage-gated potassium channel protein 4 isoform a; voltage-gated potassium channel protein KV3.4	57.1	571 e-162
			CAC19684.1	dJ1003J2.3.2 (potassium voltage-gated channel, Shaw-related subfamily, member 4)	571	571 e-162
			Q03721	CIKG_HUMAN Potassium voltage-gated channel subfamily C member 4 (Potassium channel Kv3.4) (KSHIIIC)	571	e-162 .
			AAA57263.1	potassium channel protein	. 571	e-162
٠			NP_720198.1	Shaw-related voltage-gated potassium channel protein 4 isoform b; voltage-gated potassium channel protein KV3.4	571	e-1 <u>6</u> 2
			CAC19683.1	dJ1003J2.3.1 (potassium voltage-gated channel, Shaw-related subfamily, member 4)	571	e-162
	·		NP 715624.1	Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2c	556	556 e-158
			BAC04407.1	unnamed protein product	556	556 e-158
			NP 631875.1	Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2b	556	556 e-158

H		AAL-2/2/21	AF268896 I voltage gated potassium channel Kv3.2b	556	556 e-158
ı	×	-	potassium voltage-gated potassium channel subfamily C member 2	925	556 e-158
			Shaw-related voltage-gated potassium channel protein 2 isoform KV3.2a	526	556 e-158
1	⋖	T	AF268897 1 voltage gated potassium channel Kv3.2a	556	556 e-158
F:(C-]		Q9UQR1	Z148_HUMAN Zinc finger protein 148 (Zinc finger DNA binding protein 89) (Transcription factor ZBP-89)	1460 0	· · •
	U:(IR-D) 2.34				
	-	AAC39926.1	zinc finger DNA binding protein 89 kDa	1460 0	0
	1	AAL99917.1	AF432210 1 CLL-associated antigen KW-10	1458 0	. 0
		NP_068799.1	proteir	1455 0	. 0
1	Ĭ	CAA15422.1	ZBP-89 protein	1455	0
1	-	A54693	CACCC box-binding protein ht-beta	744 0	0
ł	7	AAA36664.1	CACCC box-binding protein	743 0	0
		AAH35591.1	Similar to zinc finger protein 148 (pHZ-52)	714 0	0
	-	ABS7692.1	zinc finger binding protein homolog	695 0	0
	Ĭ	CAB70967.1	zinc finger protein	371	e-102
ł		NP 036614.1	zinc finger protein 281; ZNP-99 transcription factor	371	e-102
· .	<u> </u>	Q9Y2X9	Z281_HUMAN Zinc finger protein 281 (Zinc finger DNA binding protein 99) (Transcription factor ZBP-99) (GC-box-binding zinc finger protein 1)	371	e-102
ł		JC7089	zinc finger binding protein-99 ·	371	e-102
		AAD21084.1	zinc finger DNA binding protein 99	37.	371 e-102
ł		CAB70968.1	zinc finger protein	371	e-102
92		NP_079092.1	Fos-related antigen	621	e-177 .
$\frac{2}{2}$	U:(C-D)				
2.0 2.0 2.1	J.62 U.(IR-D) 2.1				
łI		BAB15594.1	unnamed protein product	. 621	l e-177
1				·	
	Mm.46408 F:(C-IR)	NP 004181.1	lipase, gastric	99	0 699

	. 0 899	0 699	0 699	657 0	635 0	635 0	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	474 e-133	433 e-121	431 e-121	428 e-119
ş	LIPG_HUMAN Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	triacylglycerol lipase (BC 3.1.1.3) precursor, gastric	gastric lipase precursor	gastric lipase precursor	A Chain A, Crystal Structure Of Human Gastric Lipase	B Chain B, Crystal Structure Of Human Gastric Lipase	lysosomal acid lipase	lysosomal acid lipase	Iysosomal acid lipase	AAH12287 Similar to lipase A, lysosomal acid, cholesterol esterase (Wolman disease)	lysosomal acid lipase (EC 3.1.1) / sterol esterase (EC 3.1.1.13) precursor	lysosomal acid lipase; sterol esterase	lysosomal acid lipase/cholesteryl ester hydrolase	lipase A precursor; Lipase A, lysosomal acid, cholesterol esterase	LICH_HUMAN Lysosomal acid lipase/cholesteryl ester hydrolase precursor (LAL) (Acid cholesteryl ester hydrolase) (Sterol esterase) (Lipase A) (Cholesteryl esterase)	lysosomal acid lipase/cholesteryl esterase	2 similar to bA30415.1 (novel lipase)	similar to Triacylglycerol lipase, gastric precursor (Gastric lipase) (GL)	bA304I5.1 (novel lipase)
	P07098.	S07145	CAA29413.1	CAA29414.1	1HLG	1HLG .	G01416	AAB60328.1	CAA83495.1	AAH12287.1	S41408	CAA54026.1	AAB60327.1	NP 000226.1	P38571	AAA59519.1	XP 089555.2	· XP 061222.1	CAC78754.1
-2.04 U:(C-D) 2.14 U:(TR-D) 2.27		·					·	·									<u>.</u>		
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NP_080610.1		·															:		

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WO 2005/082398 PCT/US2005/005596

286

Citation of documents herein is not intended as an admission that any of the documents cited herein is pertinent prior art, or an admission that the cited documents is considered material to the patentability of any of the claims of the present application. All statements as to the date or representation as to the contents of these documents is based on the information available to the applicant and does not constitute any admission as to the correctness of the dates or contents of these documents.

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The appended claims are to be treated as a non-limiting recitation of preferred embodiments.

In addition to those set forth elsewhere, the following references are hereby incorporated by reference, in their most recent editions as of the time of filing of this application: Kay, Phage Display of Peptides and Proteins: A Laboratory Manual; the John Wiley and Sons Current Protocols series, including Ausubel, Current Protocols in Molecular Biology; Coligan, Current Protocols in Protein Science; Coligan, Current Protocols in Immunology; Current Protocols in Human Genetics; Current Protocols in Cytometry; Current Protocols in Pharmacology; Current Protocols in Neuroscience; Current Protocols in Cell Biology; Current Protocols in Toxicology; Current Protocols in Field Analytical Chemistry; Current Protocols in Nucleic Acid Chemistry; and Current Protocols in Human Genetics; and the following Cold Spring Harbor Laboratory publications: Sambrook, Molecular Cloning: A Laboratory Manual; Harlow, Antibodies: A Laboratory Manual; Manipulating the Mouse Embryo: A Laboratory Manual; Methods in Yeast Genetics: A Cold Spring Harbor Laboratory Course Manual; Drosophila Protocols; Imaging Neurons: A Laboratory Manual; Development of Xenopus laevis: A Laboratory Manual; Using Antibodies: A Laboratory Manual; At the Bench: A Laboratory Navigator; Cells: A Laboratory Manual; Methods in Yeast Genetics: A Laboratory Course Manual; Discovering Neurons: The Experimental Basis of Neuroscience; Genome Analysis: A Laboratory Manual Series ; Laboratory DNA Science; Strategies for Protein Purification and Characterization: A Laboratory Course Manual; Genetic Analysis of Pathogenic

WO 2005/082398 PCT/US2005/005596

287

Bacteria: A Laboratory Manual; PCR Primer: A Laboratory
Manual; Methods in Plant Molecular Biology: A Laboratory
Course Manual; Manipulating the Mouse Embryo: A Laboratory
Manual; Molecular Probes of the Nervous System; Experiments
with Fission Yeast: A Laboratory Course Manual; A Short
Course in Bacterial Genetics: A Laboratory Manual and
Handbook for Escherichia coli and Related Bacteria; DNA
Science: A First Course in Recombinant DNA Technology;
Methods in Yeast Genetics: A Laboratory Course Manual;
Molecular Biology of Plants: A Laboratory Course Manual.

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All references cited herein, including journal articles or abstracts, published, corresponding, prior or otherwise related U.S. or foreign patent applications, issued U.S. or foreign patents, or any other references, are entirely incorporated by reference herein, including all data, tables, figures, and text presented in the cited references. Additionally, the entire contents of the references cited within the references cited herein are also entirely incorporated by reference.

Reference to known method steps, conventional methods steps, known methods or conventional methods is not in any way an admission that any aspect, description or embodiment of the present invention is disclosed, taught or suggested in the relevant art.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying knowledge within the skill of the art (including the contents of the references cited herein), readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present invention. Therefore, such adaptations and modifications are intended to be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the present specification is to be interpreted by the skilled artisan in light of the

WO 2005/082398 PCT/US2005/005596

288

teachings and guidance presented herein, in combination with the knowledge of one of ordinary skill in the art.

Any description of a class or range as being useful or preferred in the practice of the invention shall be deemed a description of any subclass (e.g., a disclosed class with one or more disclosed members omitted) or subrange contained therein, as well as a separate description of each individual member or value in said class or range.

The description of preferred embodiments individually shall be deemed a description of any possible combination of such preferred embodiments, except for combinations which are impossible (e.g, mutually exclusive choices for an element of the invention) or which are expressly excluded by this specification.

If an embodiment of this invention is disclosed in the prior art, the description of the invention shall be deemed to include the invention as herein disclosed with such embodiment excised.

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## CLAIMS

- 1. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of an agent which is
- (1) a polypeptide which is substantially structurally
  identical or conservatively identical in sequence to a
  reference protein which is selected from the group
  consisting of mouse and human proteins set forth in master
  table 1, subtables 1A and 1C,
- 15 or

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(2) an expression vector encoding the polypeptide of (1) above and expressible in a human cell, under conditions conducive to expression of the polypeptide of (1);

where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

- 25 2. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state which comprises administering to the subject a protective amount of an agent which is
  - (1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, or
  - (2) an anti-sense vector which inhibits expression of said polypeptide in said subject,

where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

3. A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtables 1A and 1C,

and directly correlating the level of expression of said marker gene with the propensity to progression in said patient.

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4. A method of screening for human subjects who have a propensity for progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, and inversely correlating the level of expression of said marker gene with the propensity to progression in said patient.

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- 5. The method of claims 1 or 3 in which the reference protein is of subtable 1A.
- 6. The method of claims 1 or 3 in which the reference

291

protein is of subtable 1B.

7. The method of claim 3 or 4 in which the sample is a muscle tissue sample.

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- 8: The method of any one of claims 1-7 in which the reference protein is a human protein.
- 9. The method of any one of claims 1-7 in which the 10 reference protein is a mouse protein.
  - The method of any one of claims 3 or 4 in which the level of expression of the marker protein is ascertaimed by measuring the level of the corresponding messenger RNA.

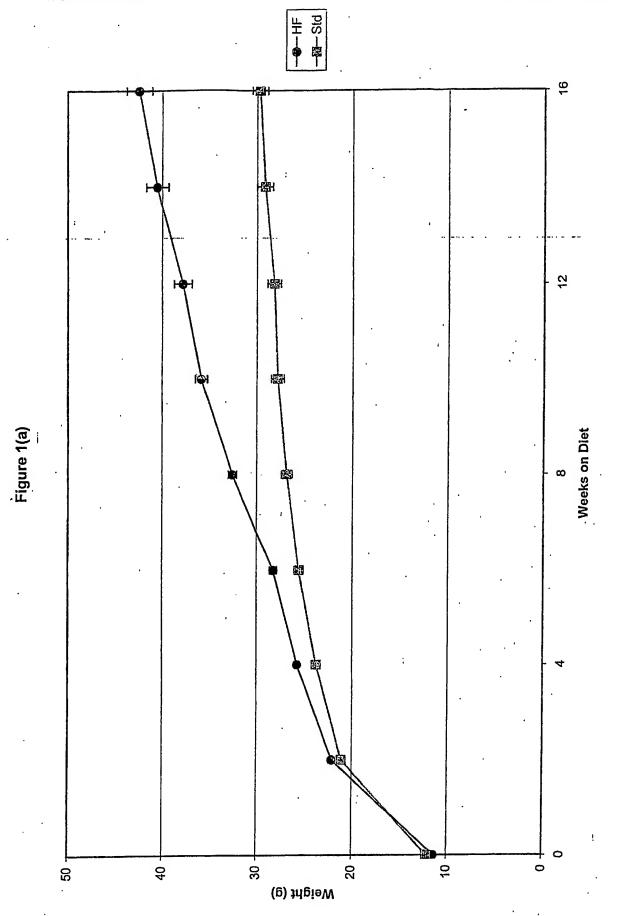
- The method of any one of claims 3 or 4in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.
- 20 12. The method of any one of claims 1-9 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein. 13. The method of any one of claims 1-10 in which said polypeptide is at least 90% identical to said reference 25 protein.
  - 14. The method of any one of claims 1-11 in which said polypeptide is identical to said reference protein.
- 15. The method of any one of claims 1-14 in which the E-30 value cited for the reference protein in Master Table 1 is not more than e-6.
- 16. The method of claim 15 in which the E-value cited for the reference protein in Master Table 1 is less than e-10. 35
  - 17. The method of claim 17 in which the E value calculated by BLASTN or BLASTX would be less than e-15, more preferably less than e-20, still more preferably less than e-40, even

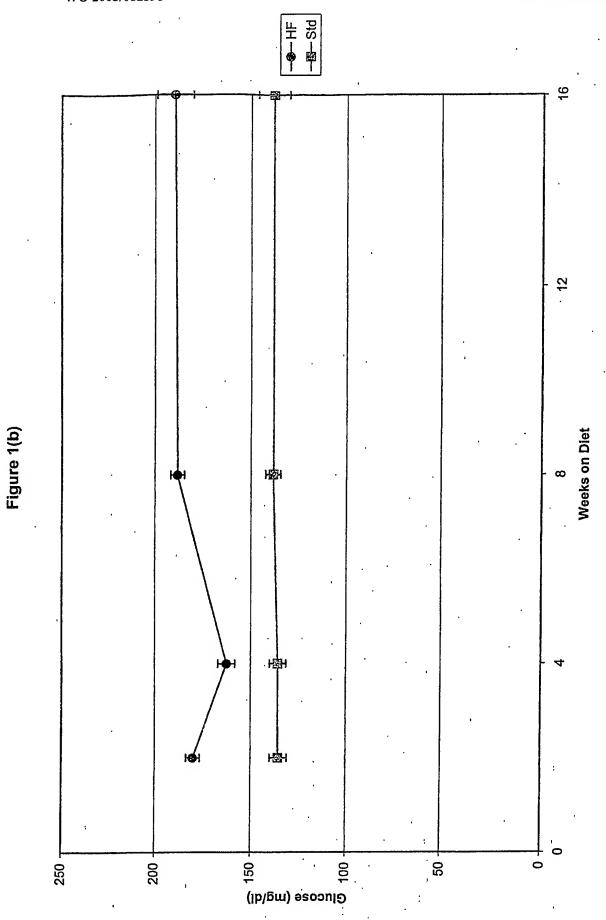
WO 2005/082398 PCT/US2005/005596

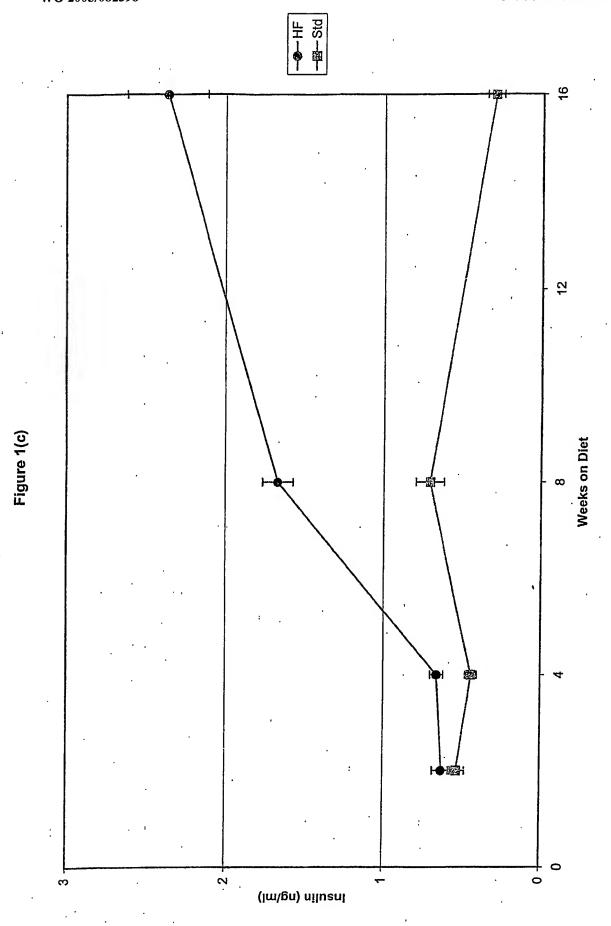
292

more preferably less than e-60, considerably more preferably less than e-80, and most preferably less than e-100.

- 18. The method of any of claims 2-17 in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.
- 19. The method of any of claims 2-17 in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.
  - 20. The method of any of claims 2-17 in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.
  - 21. The method of claim 20 in which said organic molecule is identifiable as a molecule which binds said polypeptide by screening a combinatorial library.
- 20 22. The method of claim 1 or 2 in which the agent is delivered systemically.
  - 23. The method of claim 1 or 2 in which the agent is selectively delivered to muscle tissue.







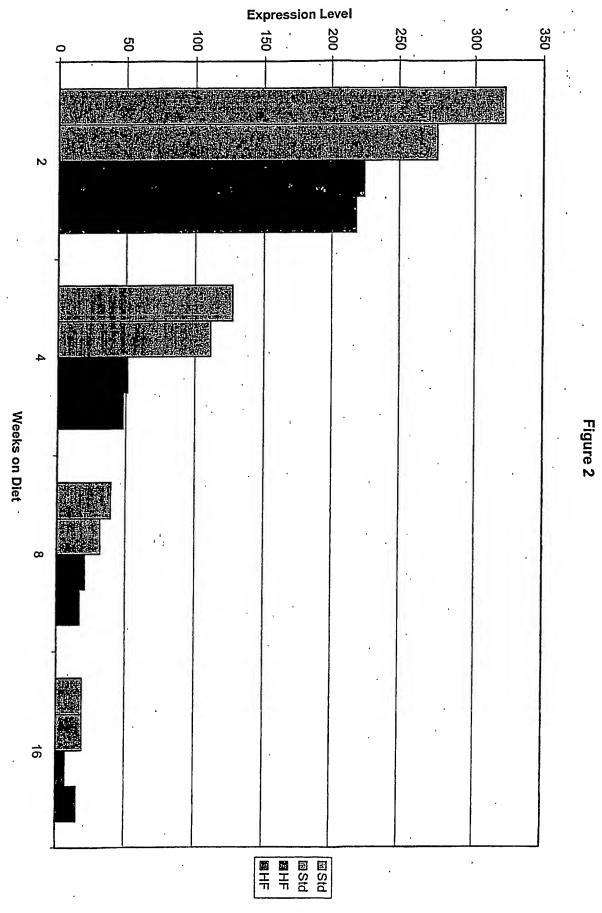
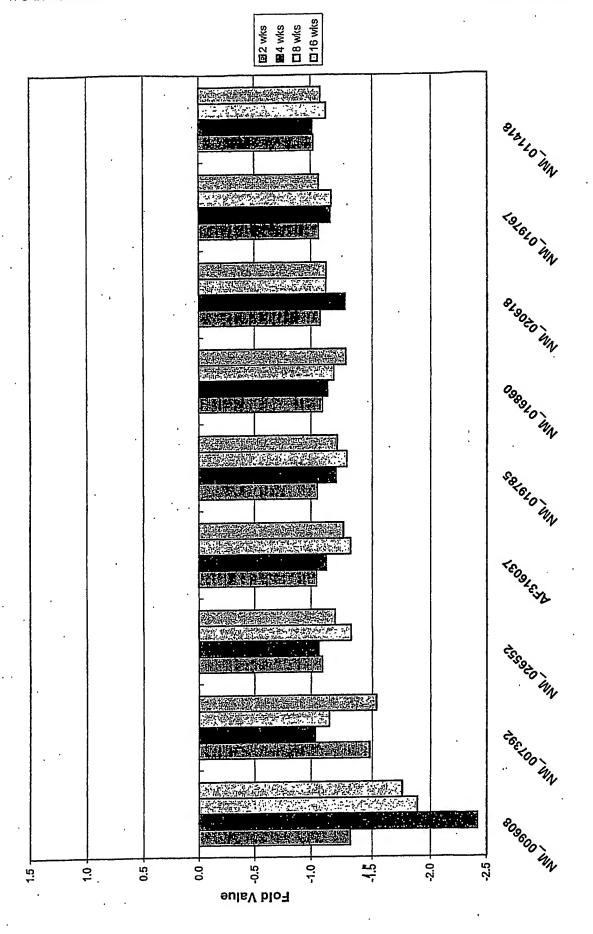
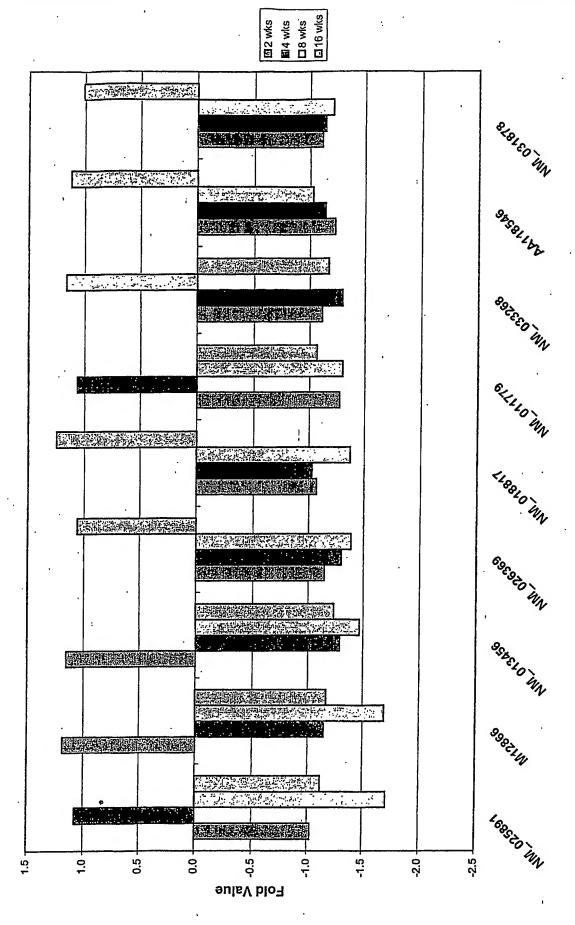


Figure 3(a)



5/6

Figure 3(b)



6/6